TORONTO NOTES

2022

COMPREHENSIVE MEDICAL REFERENCE AND A REVIEW FOR MCCQE

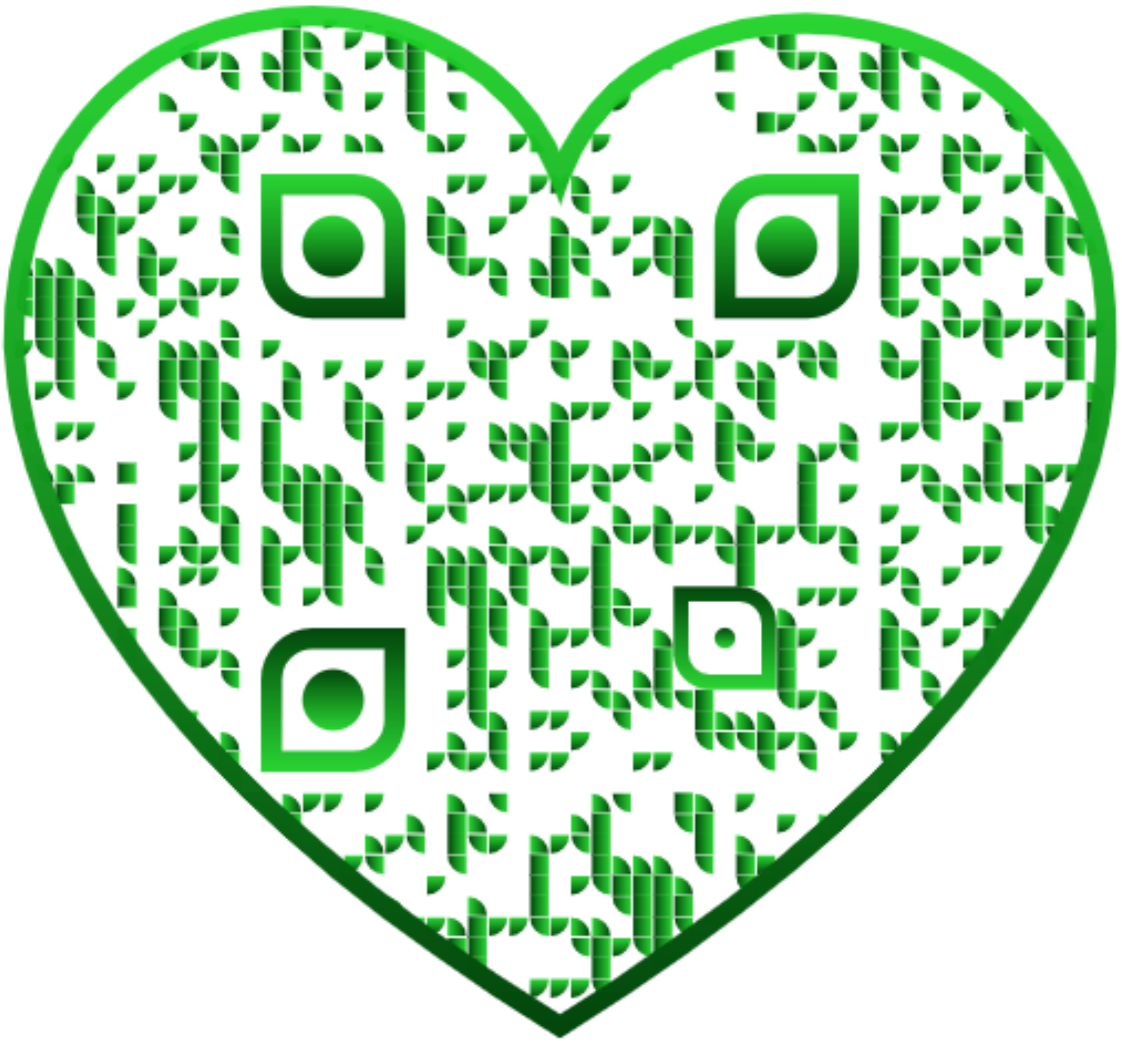
Editors-in-Chief • Yuliya Lytvyn & Maleeha A. Qazi

Associate Editors, Primary • Ming Li & Jacqui van Warmerdam

Associate Editors, Medicine • Thomas Chang & Andreea Damian

Associate Editors, Surgery • Winston W. Li & Ashmita Singh

Production Managers • Anders Erickson & Jennifer Parker



TORONTO NOTES
2022

Comprehensive Medical Reference
and a Review for the Medical Council of Canada Qualifying Exam
(MCCQE)

38th Edition

Editors-in-Chief:
Yuliya Lytvyn & Maleeha A. Qazi

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PS Psychiatry

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Diagnostic Criteria reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. © 2013 American Psychiatric Association

Acronyms

5-HT	serotonin	ECT	electroconvulsive therapy	MSE	mental status examination	SGA	second generation antipsychotics
ACh	acetylcholine	EPS	extrapyramidal symptoms	MST	magnetic stimulation therapy	SIADH	syndrome of inappropriate antidiuretic hormone secretion
ACT	assertive community treatment	ERP	exposure with response prevention	MZ	monozygotic	SNRI	serotonin and norepinephrine reuptake inhibitors
ADHD	attention deficit hyperactivity disorder	GAD	generalized anxiety disorder	NA	Narcotics Anonymous	SS	serotonin syndrome
ADL	activities of daily living	GMC	general medical condition	NMS	neuroleptic malignant syndrome	SSRI	selective serotonin reuptake inhibitor
AN	anorexia nervosa	IPT	interpersonal therapy	NOS	not otherwise specified	TCA	tricyclic antidepressant
ASD	autism spectrum disorder	IADL	instructional activities of daily living	OCD	obsessive-compulsive disorder	TD	tardive dyskinesia
ASPD	antisocial personality disorder	MBCT	mindfulness-based cognitive therapy	OCP	oral contraceptive pill	XR	extended-release
BN	bulimia nervosa	MBSR	mindfulness-based stress reduction	OCPD	obsessive-compulsive personality disorder		
CBT	cognitive behavioural therapy	MDD	major depressive disorder	ODD	oppositional defiant disorder		
CD	conduct disorder	MDE	major depressive episode	PCP	phencyclidine		
CRA	community reinforcement approach	MET	motivational enhancement therapy	PD	personality disorder		
CTO	community treatment order	MI	motivational interviewing	PDD	pervasive developmental disorder		
DA	dopamine			PTSD	post-traumatic stress disorder		
DBT	dialectical behavioural therapy			rTMS	repetitive transcranial magnetic stimulation		
DZ	dizygotic						

Psychiatric Assessment

History

Introduction
- name, role, purpose, circumstances (i.e. approximate time)
- limits of confidentiality (i.e. safety of dependents, harm to self or others)

Identifying Data
- necessary: name, age, gender (preferred pronouns), living situation (accommodation, independently, or with others), marital/relationship status, children, source of income/support, or occupation
- adjunct: outpatient/inpatient, referral source, known/unknown to provider

Chief Complaint
- in patient's own words, with duration of symptoms

History of Present Illness
- context: events, problems, stressors, losses, changes
- symptoms: onset, duration, intensity, progression, fluctuation with day/season
- impact on functioning: social, occupational, ADL/IADLs, personal care/survival
- coping strategies, treatments, personal/professional supports
- reason for seeking help that specific day
- prior episodes/experiences, longitudinal course (duration/frequency)
- last period of wellness, changes to usual personality when unwell
- opinions about cause/nature of concerns, willingness to engage, hopes/expectations of treatment

Screening Questions for Major Psychiatric Disorders
- Have you been feeling down, depressed, or hopeless?
- Do you feel anxious or worry about things?
- Has there been a time in your life where you have felt euphoric, extremely talkative, had a lot of energy, and a decreased need for sleep?
- Do you see or hear things that you think other people cannot?
- Have you ever thought of harming yourself or killing yourself?

Psychiatric Functional Inquiry
- mood: depression, mania
- other: trauma, obsessions/compulsions, disordered eating, active medical problems
- anxiety: worries, panic attacks, phobias, or social anxiety
- psychosis: hallucinations, delusions
- safety/risk: self (suicidal ideation/intent/plan (see *Suicide*, PS5), self-harm, neglect), others (homicide, aggression, violence), dependents (children, elderly, disabled, pets), driving, cooking/fires

Psychiatric Functional Inquiry

MOAPS
Mood
Other (medical problems and substance use)
Anxiety
Psychosis
Safety

Past Psychiatric History
- previous psychiatric diagnoses and mental health contacts
- hospitalizations: approximate total, date of last discharge
- emergency department visits (for mental health crisis)
- suicide attempts: number, severity, medical intervention, most recent
- self-harming behaviour (cutting)
- aggression/violence, legal (charges)
- treatments: pharmacological and non-pharmacological (effectiveness, side effects)

Substance Use History
- type: tobacco, cannabis, alcohol, other (stimulants, hallucinogens, prescription drugs, gambling/online)
- use: first, typical, last, periods of abstinence
- withdrawal symptoms (i.e. seizures, delirium tremens)
- previous treatments: counselling, detox, groups
- impact on symptoms, motivation to change

Past Medical/Surgical History
- all medical, surgical, neurological (i.e. head trauma, seizures) conditions/illnesses
- allergies

Medications
- names, doses, frequency
- adherence, effectiveness, side effects
- over the counter, supplements

Family Psychiatric/Medical History
- diagnoses, treatments, hospitalizations, suicide attempts, substance use, legal
- perceptions regarding mental illness, engagement with treatments
- if relevant: any past medical or genetic illness

Always Remember to Ask About Abuse
See Family Medicine, FM30

Past Personal/Developmental History (as relevant)
- birthplace, immigration history (if applicable), ethnicity/nationality, religion/spirituality
- family members: ages, occupations, personalities, quality of relationships
- history of verbal, physical, or sexual abuse
- prenatal and perinatal history: desired vs. unplanned pregnancy, maternal and fetal health, domestic violence, maternal substance use and exposures, complications of pregnancy/delivery
- early childhood to age 3: developmental milestones, temperament, family stability, primary caregivers/attachment figures
- middle childhood to age 11: school performance, peer relationships, bullying, activity/attention level, behavioural challenges
- late childhood to adolescence: school performance, drugs/alcohol, legal problems, peer and family relationships, extra-curriculars
- sexuality: puberty, gender identity, sexual orientation, sexual functioning/experiences, romantic relationships
- adulthood: education, employment, relationships
- hobbies, interests, sources of meaning, strengths, accomplishments, aspirations, hopes

Collateral History
- source, details provided

Mental Status Exam

General Appearance
- age (chronological vs. apparent), gender, ethnicity
- posture, grooming, hygiene, manner of dress, body habitus, distinguishing features
- eye contact, facial expression, alertness
- attitude: polite, friendly, collaborative, uncooperative, guarded/suspicious, evasive, agitated, aggressive/hostile
- reliability (consistency, congruent with collateral), ease of building rapport
- gait, psychomotor changes (slowing/agitation), tics, tremors, tardive dyskinesia, dystonia, catatonia

Mental Status Exam

ASEPTIC
Appearance and behaviour
Speech
Emotion (mood and affect)
Perception
Thought content and process
Insight and judgment
Cognition

Speech
- rate (i.e. pressured, slowed), rhythm, volume, tone, quantity, spontaneity, latency, language fluency, articulation

Mood and Affect
- mood: subjective emotional state (in patient's own words)
- affect: objective emotional state inferred from emotional responses to stimuli; described in terms of
  - quality (euthymic, depressed, elevated, anxious, irritable)
  - range (full, restricted, flat, blunted)
  - stability (continuum from fixed to labile)
  - mood congruence (inferred by comparing the patient's subjective mood with their affect)
- many clinicians use a 0-10 scale (0: worst; 10: best) when rating mood to get a subjective norm for each patient that can help to monitor changes over time and with treatment

The MSE is analogous to the physical exam. It focuses on current signs, affect, behaviour, and cognition

Spectrum of Affect
Full > Restricted > Blunted > Flat; quality (euthymic, depressed, anxious, elated)

Perception
- hallucination: sensory perception in the absence of appropriate stimuli that is similar in quality to a true perception
  - auditory (most common), visual, gustatory, olfactory, tactile
- illusion: misperception of a real external stimulus (i.e. mistaking a coat on a rack as a person late at night)
- depersonalization: change in self-awareness such that the person feels unreal, distant, or detached from their body, and/or unable to feel emotion
- derealization: feeling that the world/outer environment is unreal

There is poor correlation between clinical impression of suicide risk and frequency of attempts

Thought Process/Form
- coherence (coherent, incoherent)
- stream
  - goal-directed: clearly answers questions in a linear, organized, logical fashion
  - circumstantial: speech that is indirect and delayed in reaching its goal; eventually comes back to the point
  - tangential: speech is oblique or irrelevant; does not come back to the original point
  - loosening of associations/derailment: illogical shifting between topics
  - flight of ideas: quickly skipping from one idea to another where the ideas are marginally connected, usually associated with racing thoughts in mania
  - word salad: jumble of words lacking meaning or logical coherence
- perseveration: repetition of the same verbal or motor response to stimuli
- echolalia: repetition of phrases or words spoken by someone else
- thought blocking: sudden cessation of flow of thought and speech
- clang associations: speech based on sound such as rhyming or punning
- neologism: use of novel words or of existing words in a novel fashion

Thought Content
- major themes discussed by patient
- suicidal ideation/homicidal ideation: frequency and pervasiveness of thoughts, plan, intent, active vs. passive, protective factors
- preoccupations, ruminations: reflections/thoughts at length, not fixed or false
- obsession: recurrent and persistent thought, impulse, or image which is intrusive or inappropriate and unwanted
  - cannot be stopped by logic or reason
  - causes marked anxiety and distress
  - common themes: contamination, orderliness, sexual, pathological doubt/worry/guilt
- magical thinking (i.e. superstition, belief that thinking something will make it happen), normal in children and certain cultures
- ideas of reference: similar to delusion of reference, but less fixed (the reality of the belief is questioned)
- overvalued ideas: unusual/odd beliefs that are not of delusional proportions
- first rank symptoms of schizophrenia: thought insertion/withdrawal/broadcasting (all delusional ideas)
- delusion: a fixed false belief that is out of keeping with a person's cultural or religious background and is firmly held despite incontrovertible proof to the contrary

Insight
- ability to realize that they have a mental health concern and to appreciate its implications as it relates to functioning and benefits of treatment: none, limited, partial, or full

Judgment
- recent behaviours as they relate to safety, social functioning, treatment decisions

Cognition
- level of consciousness (alert, reduced, obtunded)
- orientation: time, place, person
- memory: immediate, recent, or remote
- global evaluation of intellect (below average, average, or above average, in keeping with person's education)
- intellectual functions: attention, concentration, calculation, abstraction (proverb interpretation, similarities test), language, communication
- MMSE/MoCA useful as standard screening assessments of cognition

Cognitive Assessment
Use MMSE to assess
- Orientation (time and place)
- Memory (immediate and delayed recall)
- Attention and concentration
- Language (comprehension, reading, writing, repetition, naming)
- Spatial ability (intersecting pentagons)

Gross screen for cognitive dysfunction: Total score is out of 30; <26 abnormal, 20-26 mild, 10-19 moderate, <10 severe

The key to differentiating between obsessions and delusions is that obsessions are usually ego dystonic, meaning unwanted and not fitting in with a person's goals and self-image, while delusions are ego syntonic

Delusions (Absolute Beliefs)
- Persecutory: belief that others are trying to cause harm to you
- Reference: interpreting ordinary, regular events/celebrities as having direct reference to you
- Erotomania: belief that another is in love with you
- Grandiose: belief that he or she has special powers, talents, or abilities
- Religious: belief of receiving instructions/powers from a higher being; of being a higher being
- Somatic: belief that you have a physical disorder/defect
- Nihilistic: belief that things do not exist; a sense that everything is not real

Assessing Insight and Judgment
Insight
- Acknowledgment of symptoms as a departure from baseline or source of suffering
- Attribution of symptoms to illness or acceptance as such explanation as part of the process
- Acknowledgement of need for treatment (Why are you in the hospital? Why are you taking this medication? What would happen if you stopped taking it?)

Judgment
Can be observed from collected history and patient's appearance and actions. Are they:
- Dressed appropriately for the weather?
- Acting appropriately in the given situation?
- Taking care of self and/or dependents?

Assessment and Plan

Historical Multiaxial Model
- since DSM-5, this model is no longer used for psychiatric diagnosis. Instead, relevant psychiatric and medical diagnoses are simply listed. Nevertheless, we offer it here as a possible framework for psychiatric patient assessment, as many physicians still employ it

Multiaxial Assessment
- Axis I: DSM-5 diagnoses (preferred and differential)
- Axis II: personality disorders, intellectual disability
- Axis III: medical conditions potentially relevant to understanding/management of the mental disorder
- Axis IV: psychosocial and environmental issues
- Axis V: Global Assessment of Functioning (GAF, 0 to 100) incorporating effects of axes I to IV

After History and MSE, the assessment and plan is recorded

Assessment/Problem Formulation
- identify predominant symptom cluster (mood, anxiety, psychosis) that causes the most distress/interference and persists when other symptom categories are not present (i.e. psychosis in the absence of mood symptoms)
- dominating symptoms will direct differential
- consider current issues as they relate to an individual considering three domains: biological, psychological, and social
- for each category: predisposing, precipitating, perpetuating, and protecting factors are considered

Always rule out substance use and other medical causes before considering psychiatric causes

Approach to Management
- consider short-term and long-term, and three types: biological (i.e. pharmacotherapy, ECT), psychological (i.e. CBT), and social (i.e. supports, finance/employment/return to work, housing, social activity, recreation, medication/psychotherapy coverage)

Suicide

Importance
- must be screened for in every encounter; part of risk assessment along with violent/homicidal ideation

Suicidal Ideation Assessment
- Asking patients about suicide will not give them the idea or the incentive to die by suicide
- The best predictor of completed suicide is a history of attempted suicide
- The most common psychiatric disorders associated with completed suicide are mood disorders and alcohol use disorders

Approach
- ask every patient: i.e. "Have you had any thoughts of wanting to harm or kill yourself?"
- classify ideation
  - passive ideation ("death wish"): where patient would rather not be alive but currently has no active plan for suicide
    - i.e. "I would rather not wake up" or "I would not mind if a car hit me"
  - active ideation
    - i.e. "I think about killing myself"
- assess risk
  - plan: "Do you have a plan as to how you would end your life?"
  - intent: "Do you think you would actually carry out this plan?" "If not, why not?"
  - past attempts: number, lethality, outcome, medical intervention, while intoxicated?, precipitants
  - if intoxicated on the first approach, reassess when sober
- assess suicidal ideation
  - onset and frequency of thoughts: "When did this start?" or "How often do you have these thoughts?"
  - control over suicidal ideation: "How do you cope when you have these thoughts?" "Could you call someone for help?"
  - intention: "Do you want to end your life?" or "Do you wish to kill yourself?"
  - intended lethality: "What do you think would happen if you actually took those pills?"
  - access to means: "How will you get a gun?" or "Which bridge do you think you would go to?"
  - time and place: "Have you picked a date and place? Is it in an isolated location?"
  - provocative factors: "What makes you feel worse (i.e. being alone)?"
  - protective factors: "What keeps you alive (i.e. friends, family, pets, faith, therapist)?"
  - final arrangements: "Have you written a suicide note? Made a will? Given away your belongings?"
  - practiced suicide or aborted attempts: "Have you ever put the gun to your head?" "Held the medications in your hand?" "Stood at the bridge?"
  - ambivalence: "I wonder if there is a part of you that wants to live, given that you came here for help?"
  - determine level of risk and develop treatment/safety plan

Suicide Risk Factors

SAD PERSONS
Sex (male)
Age >60 yr
Depression
Previous attempts
Ethanol abuse
Rational thinking loss (delusions, hallucinations, hopelessness)
Suicide in family
Organized plan
No spouse (no support systems)
Serious illness, intractable pain

Assessment of Suicide Attempt
- setting (isolated vs. others present/chance of discovery)
- planned vs. impulsive attempt, triggers/stressors
- substance use/intoxication
- medical attention (brought in by another person vs. brought in by self to ED)
- time lag from suicide attempt to ED arrival
- expectation of lethality, dying
- reaction to survival (guilt/remorse vs. disappointment/self-blame)
- evidence of escalation in potential lethal means

Epidemiology
- attempted:completed = 20:1 (100:1 in younger persons; 4:1 in older persons)
- M:F=1:4 for attempts, 3:1 for completed

Risk Factors

- epidemiologic factors
  - age: increases after age 14, second most common cause of death for ages 15-24, highest rates of completion in persons >75 yr
  - sex: male
  - race/ethnic background: White people or Indigenous peoples in Canada
  - marital status: widowed/divorced
  - living situation: alone; no children <18 y/o in the household
  - other: stressful life events, or access to firearms
- psychiatric factors
  - past suicide attempt(s)
  - eating disorders
  - bipolar disorder
  - major depression
  - mixed drug misuse
  - panic disorder
  - schizophrenia
  - personality disorder
  - alcohol use
- psychosocial factors
  - recent, severe stressful life event (relationship, financial, trauma)
- psychiatric disorders
  - mood disorders (15% lifetime risk in depression; higher in bipolar)
  - anxiety disorders (especially panic disorder)
  - schizophrenia (10-15% risk)
  - substance use disorder (especially alcohol – 15% lifetime risk)
  - eating disorders (5% lifetime risk)
  - adjustment disorder
  - conduct disorder
  - personality disorders (borderline, antisocial)
- past history
  - prior suicide attempt(s), most recent attempt
  - family history of suicide attempt/completion

Clinical Features

- symptoms associated with suicide:
  - hopelessness
  - anhedonia
  - insomnia
  - severe anxiety
  - impaired concentration
  - psychomotor agitation

Management

- proper documentation of the clinical encounter and rationale for management is essential
- for higher risk patients (with a plan and intention to act, have access to lethal means, recent social stressors, and symptoms suggestive of a psychiatric disorder)
  - hospitalization should be strongly considered
  - do not leave patient alone; remove potentially dangerous objects from room
  - if patient refuses to be hospitalized, complete form for involuntary admission (Form 1) and must give patient Form 30 to notify them of their admission (in Ontario)
- for lower risk patients (not actively suicidal, with no active plan, or access to lethal means)
  - discuss protective factors and supports in their life, remind them of what they live for, promote survival skills that helped them through previous suicide attempts
  - make a safety plan that could include an agreement that they will:
    - not harm themselves
    - avoid alcohol, drugs, and situations that may trigger suicidal thoughts
    - follow-up with you at a designated time
    - contact a health care worker, call a crisis line, or go to an emergency department if they feel unsafe or if their suicidal feelings return or intensify
- patients with depression: consider hospitalization if symptoms severe or if psychotic features are present; otherwise outpatient treatment with good supports and pharmacotherapy
- patients with alcohol- or substance-related issues: suicidality usually resolves with abstinence for a few days; if not, suspect depression
- patients with personality disorders: crisis intervention, may or may not hospitalize
- patients with schizophrenia/psychosis: hospitalization might be necessary
- patients with parasuicidal behaviours/self-mutilation: long-term psychotherapy with brief crisis intervention when necessary

Psychotic Disorders

Definition
- characterized by a significant impairment in reality testing
- positive symptoms
  - delusions or hallucinations (with or without insight into their pathological nature)
  - grossly disorganized or abnormal motor behaviours (including catatonia)
  - formal thought disorder
- negative symptoms of schizophrenia
  - diminished emotional expression (i.e. affective flattening)
  - anhedonia
  - avolition
  - alogia
  - asociality

Differential Diagnosis of Psychosis

Approach
- differentiate among psychotic disorders and distinguish them from other primary diagnoses with psychotic features
- consider symptoms, persistence, and time
- symptoms: the primary diagnosis needs full criteria to be met
  - mood: depressive episodes with psychotic features, manic episodes with psychotic features
  - psychotic: consider symptoms in Criterion A of schizophrenia (see *Criteria for Schizophrenia*, PS8)
- persistence: is there a time when certain symptom clusters are present without other clusters?
  - i.e. if there is a period of time with mood symptoms but not psychotic symptoms, consider mood disorder
  - i.e. if psychotic symptoms occur only with mood symptoms, consider mood disorder with psychotic features
  - i.e. if during a 2 wk period where psychotic symptoms persist in the absence of mood symptoms, consider schizoaffective disorder
  - i.e. if long periods with psychotic symptoms and brief or rare mood symptoms, consider schizophrenia
- time: how long have the symptoms been present?

Table 1. Differentiating Psychotic Disorders

Disorder	Psychotic Symptoms	Duration
Brief Psychotic Disorder	≥1 positive symptoms of criterion A	<1 mo with eventual full return to premorbid functioning
Schizophreniform Disorder	Criterion A	1-6 mo
Schizophrenia	Criterion A	>6 mo
Schizoaffective Disorder	Criterion A + major mood episode (MDE or manic), ≥2 wk of psychotic symptoms without mood symptoms	>1 mo
Delusional Disorder	One or more delusions (if hallucinations, related to delusional theme)	>1 mo
Substance-Induced Psychotic Disorder	Delusions or hallucinations	Onset during intoxication/withdrawal, resolve in <1 mo without use
2° to Mood Disorder	Mood symptoms dominant + delusions/ hallucinations (mood congruent)	Psychosis may be present only for the duration of the mood episode

Relevant Investigations
- CBC, electrolytes (including extended electrolytes), creatinine, glucose, urinalysis, urine drug screen, TSH, and vitamin B_{12}
- LFTs, fasting lipids, HbA1C to obtain baseline levels prior to antipsychotic initiation
- ECG (several antipsychotics affect cardiac conduction)
- if clinically indicated, order infectious work-up, inflammatory markers, and brain imaging

Delusions: fixed, false beliefs that are not amenable to change in light of conflicting evidence
Hallucinations: perceptual experiences occurring without an external stimulus

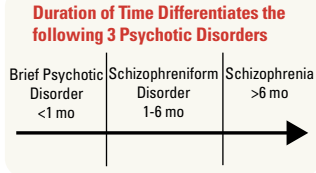

Figure 1. Differentiating psychotic disorders by duration

DDx for Psychosis
- Primary psychotic disorders: schizophrenia, schizophreniform, brief psychotic, schizoaffective, delusional disorder
- Mood disorders: MDD with psychotic features, bipolar disorder (manic or depressive episode with psychotic features)
- Personality disorders: schizotypal, schizoid, borderline, paranoid, obsessive-compulsive (they predispose to psychosis but presence of psychotic symptoms require another diagnosis)
- General medical conditions: tumour, head trauma, dementia, delirium, metabolic, infection, stroke, temporal lobe epilepsy
- Substance-induced psychosis: onset during intoxication or withdrawal, prescribed medications, toxins

Management of Acute Psychosis and Mania
- Ensure safety of self, patient, and other patients
- Have an exit strategy
- Decrease stimulation
- Assume a non-threatening stance
- IM medications (benzodiazepine and antipsychotic) often needed as patient may refuse oral medication
- Physical restraints may be necessary
- Do not use antidepressants or stimulants

Schizophrenia

DSM-5 DIAGNOSTIC CRITERIA FOR SCHIZOPHRENIA

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A. two (or more) of the following, each present for a significant portion of time during a 1 mo period (or less if successfully treated). At least one of these must be (1), (2), or (3)
   1. delusions
   2. hallucinations
   3. disorganized speech (e.g. frequent derailment or incoherence)
   4. grossly disorganized or catatonic behaviour
   5. negative symptoms (i.e. diminished emotional expression or avolition)

B. for a significant portion of time since the onset of the disturbance, level of functioning in one or more major areas (e.g. work, interpersonal relations, self-care) is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning)

C. continuous signs of the disturbance persist for at least 6 mo. This 6 mo period must include at least 1 mo of symptoms (or less if successfully treated) that meet Criterion A (i.e. active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or by two or more symptoms listed in Criterion A present in an attenuated form (e.g. odd beliefs, unusual perceptual experiences)

D. schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either 1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or 2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness

E. the disturbance is not attributable to the physiological effects of a substance (e.g. drug of abuse, medication) or another medical condition

F. if there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia are also present for at least 1 mo (or less if successfully treated)

- **specifiers**: type of episode (e.g. first episode, multiple episodes, continuous), in acute episode/partial/full remission, with catatonia, current severity based on quantitative assessment of primary symptoms of psychosis

Epidemiology

- prevalence: 0.3-0.7%, M:F=1:1
- mean age of onset: females late-20s with a 2nd peak in mid-life; males early- to mid-20s (some cases with late onset)
- suicide risk: 5-6% die by suicide, 20% attempt suicide

Etiology

- multifactorial: disorder is a result of interaction between both biological and environmental factors
  - genetic: 40% concordance in monozygotic (MZ) twins; 46% if both parents have schizophrenia; 10% of dizygotic (DZ) twins, siblings, children affected; vulnerable genes include Disrupted-in-Schizophrenia 1 (DISC1); neuregulin 1 (NRG 1); dystrobrevin binding protein/dysbindin (DTNBP1); catechol-O-methyltransferase (COMT); d-amino acid oxidase activator (DAOA); metabotropic glutamate receptor 3 (GRM3); and brain-derived neurotrophic factor (BDNF)
  - neurochemistry ("dopamine hypothesis"): excess activity in the mesolimbic dopamine pathway may mediate the positive symptoms of psychosis, while decreased dopamine in the prefrontal cortex may mediate negative and cognitive symptoms. GABA, glutamate, and ACh dysfunction are also thought to be involved
  - neuroanatomy: decreased frontal lobe function; asymmetric temporal/limbic function; decreased basal ganglia function; subtle changes in thalamus, cortex, corpus callosum, and ventricles; cytoarchitectural abnormalities
  - neuroendocrinology: abnormal growth hormone, prolactin, cortisol, and ACTH
  - neuropsychology: global defects seen in attention, language, and memory suggest disrupted connectivity of neural networks
  - environmental: indirect evidence of cannabis use, geographical variance, winter season of birth, obstetrical complications, and prenatal viral exposure

Pathophysiology

- neurodegenerative theory: natural history may be a rapid or gradual decline in function and ability to communicate
  - glutamate system may mediate progressive degeneration by excitotoxic mechanism which leads to production of free radicals
- neurodevelopmental theory: abnormal development of the brain from prenatal life
  - neurons fail to migrate correctly, make inappropriate connections, and undergo apoptosis in later life

Relationship Between Duration of Untreated Psychosis (DUP) and Outcome in First-Episode Schizophrenia
Am J Psychiatry 2005;162:1785-1804
Purpose: To review the association between DUP and symptom severity at first treatment contact, and between DUP and treatment outcomes.
Methods: Critical review and meta-analysis of studies involving patients with non-affective psychotic disorders at or close to first treatment.
Results: 43 studies with 4177 patients were included. Shorter DUP was associated with greater response to antipsychotic treatment, as measured by global psychopathology, positive symptoms, negative symptoms, and functional outcomes. At the time of treatment initiation, longer DUP was associated with the severity of negative symptoms but not with the severity of positive symptoms, global psychopathology, or neurocognitive function.
Conclusions: DUP may be a potentially modifiable prognostic factor.

Duration of Untreated Psychosis as Predictor of Long-term Outcome in Schizophrenia: Systematic Review and Meta-analysis
Brit J Psychiatry 2014;205:88-94
Purpose: To review the association between DUP and long-term outcomes of schizophrenia.
Methods: A systematic review and meta-analysis on the effects of duration of untreated psychosis on clinical, social, or quality of life outcomes at least 2 yr following psychosis in people with schizophrenia.
Results: 33 studies were included. Longer DUP was associated with poorer general symptomatic outcome, more severe positive and negative symptoms, lesser likelihood of remission, and poorer social functioning and global outcomes. Longer DUP was not associated with employment, quality of life, or hospital treatment.

Disorganized Behaviours in Schizophrenia

- Catatonic stupor: fully conscious but mute, unresponsive, immobile, and maintaining bizarre positions for a long time
- Catatonic excitement: uncontrolled and aimless motor activity, extreme agitation
- Stereotypy: repeated but non-goal-directed movement (i.e. rocking)
- Mannerisms: goal-directed activities that are odd or out of context (i.e. grimacing)
- Echopraxia: imitates movements and gestures of others
- Automatic obedience: carries out simple commands in robot-like fashion
- Negativism: refuses to cooperate with simple requests for no apparent reason
- Inappropriate affect, neglect of self-care, other odd behaviours (random shouting)

Comorbidity
- substance use disorders (>50% use tobacco)
- anxiety disorders
- reduced life expectancy secondary to medical comorbidities (i.e. obesity, diabetes, metabolic syndrome, CV/pulmonary disease)

Management of Schizophrenia
- biological/somatic
  - acute treatment and maintenance: antipsychotics (risperidone, aripiprazole, haloperidol, paliperidone; clozapine if resistant); regimens of IM q2-4 wk. Long-acting injectables (LAI or depot) shown to be more effective in reducing relapse and rehospitalization compared with oral alternatives
  - adjunctive: ± mood stabilizers (for aggression/impulsiveness - lithium, valproate, carbamazepine) ± anxiolytics ± ECT
  - maintenance treatment for at least 1-2 yr after the first episode, at least 5 yr after multiple episodes (relapse causes severe deterioration)
- psychosocial
  - psychotherapy (individual, family, group), supportive, CBT (see Table 14, PS51)
  - ACT (Assertive Community Treatment): mobile mental health teams that provide individualized treatment in the community and help patients with medication adherence, basic living skills, social support, job placements, resources
  - social skills training, employment programs, disability benefits
  - housing (group home, boarding home, transitional home)

Course and Prognosis
- majority of individuals display some type of prodromal phase
- course is variable: some individuals have exacerbations and remissions while others remain chronically ill; accurate prediction of the long-term outcome is not possible
- positive symptoms typically diminish with treatment; negative symptoms tend to be most persistent and cognitive symptoms may not improve
- over time: 1/3 improve, 1/3 remain the same, 1/3 worsen

Cannabis Use and Earlier Onset of Psychosis
Arch Gen Psychiatry 2011;68:555-561
Purpose: To examine the extent to which cannabis, alcohol, and other psychoactive drugs affect the age of onset of psychosis.
Method: A systematic review and meta-analysis. English studies were included that compared two cohorts: patients who used substances vs. patients who did not use substances.
Results: 83 studies were included. The age of onset in cannabis users was 2.7 yr younger than in nonusers. For broadly defined substance use, age of onset of psychosis was 2.0 yr earlier than for nonusers. Alcohol use was not associated with significantly earlier age of psychosis.
Conclusions: These results provide evidence that cannabis plays a role in earlier onset of psychosis.

Good Prognostic Factors
- Acute onset
- Later age of onset
- Shorter duration of prodrome
- Female gender
- Good cognitive functioning
- Good premorbid functioning
- No family history
- Presence of affective symptoms
- Absence of structural brain abnormalities
- Good response to drugs
- Good support system

Schizophreniform Disorder

Diagnosis
- criteria A, D, and E of schizophrenia are met; an episode of the disorder lasts for > 1 mo but < 6 mo
  - if the symptoms have extended past 6 mo the diagnosis becomes schizophrenia
  - specifiers: with/without good prognostic features (e.g. acute onset, confusion/perplexity, good premorbid functioning, absence of blunt/flat affect), with catatonia, current severity based on quantitative assessment of primary symptoms of psychosis

Treatment
- similar to acute schizophrenia

Prognosis
- better than schizophrenia; 1/3 recover within 6 mo, 2/3 progress to schizophrenia

Brief Psychotic Disorder

Diagnosis
- criteria A1-A4, D, and E of schizophrenia are met; an episode lasts for at least 1 d, but less than 1 mo with eventual full return to premorbid level of functioning
- specifiers: with/without marked stressors, with postpartum onset, with catatonia, current severity
- can occur after a stressful event or postpartum (see *Postpartum Mood Disorders*, PS14)

Treatment
- secure/safe environment, antipsychotics, and anxiolytics

Prognosis
- good, self-limiting, should return to pre-morbid function within 1 mo

Schizoaffective Disorder

DSM-5 DIAGNOSTIC CRITERIA FOR SCHIZOAFFECTIVE DISORDER

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A. an uninterrupted period of illness during which there is a major mood episode concurrent with Criterion A of schizophrenia
B. delusions or hallucinations for 2 or more wk in the absence of a major mood episode during the lifetime duration of the illness
C. symptoms that meet criteria for a major mood episode are present for the majority of the total duration of the active and residual periods of the illness
D. the disturbance is not attributable to the effects of a substance or another medical condition

- **specifiers**: bipolar type, depressive type, with catatonia, type of episode (i.e. first episode, multiple episode), severity

Non-bizarre delusions involve situations that could occur in real life (i.e. being followed, poisoned, loved at a distance) Bizarre delusions involve situations that cannot occur in real life (i.e. being kidnapped by aliens, having one's organs stolen)

Epidemiology

- one-third as prevalent as schizophrenia; schizoaffective disorder bipolar type more common in young adults, schizoaffective disorder depressive type more common in older adults
- depressive symptoms correlated with higher suicide risk (lifetime risk 5%)

Treatment

- antipsychotics, mood stabilizers, and antidepressants

Prognosis

- between that of schizophrenia and of mood disorder

Delusional Disorder

DSM-5 DIAGNOSTIC CRITERIA FOR DELUSIONAL DISORDER

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A. the presence of one (or more) delusions with a duration of 1 mo or longer
B. criterion A for schizophrenia has never been met
   Note: hallucinations, if present, are not prominent and are related to the delusional theme
C. apart from the impact of the delusion(s) or its ramifications, functioning is not markedly impaired, and behaviour is not obviously bizarre or odd
D. if manic or major depressive episodes have occurred, these have been brief relative to the duration of the delusional periods
E. the disturbance is not attributable to the physiological effects of a substance or another medical condition and is not better explained by another mental disorder

- **subtypes**: erotomanic, grandiose, jealous, persecutory, somatic, mixed, unspecified
- **further specify**: bizarre content, type of episode (e.g. first episode, multiple episode), severity

Treatment

- antipsychotics, psychotherapy, and antidepressants

Prognosis

- may respond well to antipsychotics but most patients refuse them and have chronic, unremitting course; some maintain a high level of functioning; some progress to schizophrenia

Mood Disorders

Definitions

- accurate diagnosis of a mood disorder requires a careful past medical and psychiatric history to detect past mood episodes and to rule out whether these episodes were secondary to substance use, a medical condition, etc.
- mood episodes represent a combination of symptoms comprising a predominant mood state that is abnormal in quality or duration (i.e. major depressive, manic, mixed, hypomanic). DSM-5 Criteria for mood episodes are listed below
- types of mood disorders include:
  - depressive (MDD, persistent depressive disorder)
  - bipolar (bipolar I/II disorder, cyclothymia)
  - induced by or due to ("secondary to") a general medical condition, substance, medication, or other psychiatric condition

Medical Workup of Mood Disorder

- routine screening: physical exam, CBC, extended electrolytes, LFT, renal and thyroid function tests, drug screen, medications list
- additional screening: B_{12} (in older people), neurological consultation, chest x-ray, ECG, head imaging

Mood Episodes

DSM-5 DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE EPISODE

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A. ≥5 of the following symptoms have been present during the same 2 wk period and represent a change from previous functioning; at least one of the symptoms is either 1) depressed mood or 2) loss of interest or pleasure (anhedonia)
   Note: Do not include symptoms that are clearly attributable to another medical condition
   - depressed mood most of the day, nearly every day, as indicated by either subjective report or observation made by others
   - markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
   - significant and unintentional weight loss/weight gain, or decrease/increase in appetite nearly every day
   - insomnia or hypersomnia nearly every day
   - psychomotor agitation or retardation nearly every day
   - fatigue or loss of energy nearly every day
   - feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
   - diminished ability to think or concentrate, or indecisiveness, nearly every day
   - recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
B. the symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
C. the episode is not attributable to the direct physiological effects of a substance or a GMC

Criteria for Depression (≥5)

MSIGECAPS
Mood: depressed
Sleep: increased/decreased
Interest: decreased
Guilt
Energy: decreased
Concentration: decreased
Appetite: increased/decreased
Psychomotor: agitation/retardation
Suicidal ideation

DSM-5 CRITERIA FOR MANIC EPISODE

Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 2013. American Psychiatric Association

A. a distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy, lasting ≥1 wk and present most of the day, nearly every day (or any duration if hospitalization is necessary)
B. during the period of mood disturbance and increased energy or activity, ≥3 of the following symptoms have persisted (4 if the mood is only irritable) and have been present to a significant degree and represent a noticeable change from usual behaviour
   - inflated self-esteem or grandiosity
   - decreased need for sleep (e.g. feels rested after only 3 h of sleep)
   - more talkative than usual or pressure to keep talking
   - flight of ideas or subjective experience that thoughts are racing
   - distractibility (i.e. attention too easily drawn to unimportant or irrelevant external stimuli)
   - increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
   - excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g. engaging in unrestrained shopping sprees, sexual indiscretions, or foolish business investments)
C. the mood disturbance is sufficiently severe to cause marked impairment in social or occupational functioning or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features
D. the episode is not attributable to the physiological effects of a substance or another medical condition
   Note: A full manic episode that emerges during antidepressant treatment but persists at a fully syndromal level beyond the physiological effect of that treatment is sufficient evidence for a manic episode, and therefore, a bipolar I diagnosis
   Note: Criteria A-D constitute a manic episode. At least one lifetime manic episode is required for the diagnosis of bipolar I disorder

Criteria for Mania (≥3)

GST PAID
Grandiosity
Sleep (decreased need)
Talkative
Pleasurable activities, Painful consequences
Activity (increased)
Ideas (flight of)
Distractible

Hypomanic Episode

- criterion A and B of a manic episode is met, but duration is ≥4 d
- episode associated with an unequivocal change in functioning that is uncharacteristic of the individual when not symptomatic and observable by others
- episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization
- absence of psychotic features (if these are present the episode is, by definition, manic)

Mixed Features
- episode specifier in a manic, hypomanic, or depressive episode of BDI/II that indicates the presence of both depressive and manic symptoms concurrently, classified by the disorder and primary mood episode (i.e. BDI, current episode manic, with mixed features)
- clinical importance due to increased suicide risk and appropriate treatment
- if found in patient diagnosed with major depression, there is a high index of suspicion for BD
- while meeting the full criteria for a MDE, the patient has on most days ≥3 of criteria B for a manic episode
- while meeting the full criteria for a manic/hypomanic episode, the patient has on most days ≥3 of criteria A for a depressive episode (the following criterion A cannot count: psychomotor agitation, insomnia, difficulties concentrating, or weight changes)

Depressive Disorders

MAJOR DEPRESSIVE DISORDER

DSM-5 DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE DISORDER (MDD)
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A. presence of a single MDE (vs. recurrent, which requires presence of two or more MDEs; to be considered separate episodes, there must be an interval of at least 2 consecutive mo in which criteria are not met for a MDE)
B. the MDE is not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder NOS
C. there has never been a manic episode or a hypomanic episode

- **Note**: This exclusion does not apply if all of the manic-like, or hypomanic-like episodes are substance or treatment-induced or are due to the direct physiological effects of another medical condition
- **specifiers**: with anxious distress, mixed features, melancholic features, atypical features, mood-congruent psychotic features, mood-incongruent psychotic features, catatonia, peripartum onset, seasonal pattern

Antidepressants for Depression in Physically Ill People
Cochrane DB Syst Rev 2010;CD007503
Purpose: To determine the efficacy of antidepressants in treating depression in people with comorbid physical illness.
Methods: Systematic review of RCTs comparing the efficacy of antidepressants vs. placebo in the treatment of major depression, adjustment disorder, and dysthymia in adults with comorbid depression and physical illness. Physical illness was defined as any medical condition known to have a biological underpinning where diagnosis is not purely symptom based.
Results: Fifty-one studies including 3603 participants were included in this review. Both tricyclic antidepressants and selective serotonin reuptake inhibitors were more effective than placebo at treating depression in adults with concurrent physical illness. Dry mouth and sexual dysfunction were more common in patients treated with an antidepressant.

Epidemiology
- Canadian annual/lifetime prevalence: 5%/11%
- peak prevalence age 15-25 yr (M:F=1:2)

Etiology
- biological
  - genetic: 65-75% MZ twins; 14-19% DZ twins, 2-4 fold increased risk in first-degree relatives
  - neurotransmitter dysfunction: decreased activity of 5-HT, NE, and DA at neuronal synapse; changes in GABA and glutamate; various changes detectable by fMRI
  - neuroendocrine dysfunction: abnormal HPA axis activity
  - neuroanatomy and neurophysiology: decreased hippocampal volume, increased size of ventricles; decreased REM latency and slow-wave sleep; increased REM length
  - immunologic: increased pro-inflammatory cytokines IL-6 and TNF
  - secondary to medical condition, medication, substance use disorder
- psychosocial
  - cognitive (i.e. distorted schemata, Beck's cognitive triad: negative views of oneself, the world, and the future)
  - environmental factors (i.e. job loss, bereavement, history of abuse or neglect, early life adversity)
  - comorbid psychiatric diagnoses (i.e. anxiety, substance use disorder, developmental disability, dementia, eating disorder)

Risk Factors
- sex: F:M=2:1
- family history: depression, alcohol use disorder, suicide attempt or completion
- childhood experiences: loss of parent before age 11, negative home environment (abuse, neglect)
- personality: neuroticism, insecure, dependent, obsessional
- recent stressors: illness, financial, legal, relational, academic
- lack of intimate, confiding relationships or social isolation
- low socioeconomic status

Clinically Significant Depressive Symptoms in the Elderly
- affects about 15% of community residents >65 y/o; up to 50% in nursing homes
- high suicide risk due to social isolation, chronic medical illness, and decreased independence
- suicide peak: males ages 80-90, females ages 50-65
- low mood or dysphoria may not be a reliable indicator of depression in those >70 y/o
- often present with somatic complaints (i.e. changes in weight, sleep, energy; chronic pain) or anxiety symptoms
- may have prominent cognitive changes after onset of mood symptoms (dementia syndrome of depression)
- see Table 3, PS26, for a comparison of delirium and dementia

Treatment
- lifestyle: increased aerobic exercise, mindfulness-based stress reduction, sleep hygiene
- biological: SSRIs, SNRIs, other antidepressants, somatic therapies (see *Pharmacotherapy*, PS52 and *Somatic Therapies*, PS61)
  - for MDE of moderate or greater severity, 1st line pharmacotherapy are used: most 2nd generation antidepressants, with escitalopram, mirtazapine, sertraline, venlafaxine, agomelatine and citalopram showing evidence for superiority
  - for non or partial response, optimize the dose, switch to antidepressant with superiority, or add augmenting agent (i.e. aripiprazole, quetiapine, risperidone)
  - typical response to antidepressant treatment: physical symptoms improve at 2 wk, mood/cognition by 4 wk; if no improvement after 4 wk at the highest tolerated therapeutic dosage, alter regimen
  - ECT: currently fastest and most effective treatment for MDD. Consider in severe, psychotic, or treatment-resistant cases
  - rTMS: 1st line treatment for MDD for patients who have failed at least 1 antidepressant treatment. Efficacy equivalent to medications (but not to ECT) with good safety and tolerability
  - phototherapy: especially if seasonal component, shift work, sleep dysregulation
- psychological
  - individual therapy (CBT, interpersonal, behavioural activation, dynamic), group therapy, family therapy
- social: vocational rehabilitation, social skills training
- experimental: magnetic seizure therapy, deep brain stimulation, ketamine

Prognosis
- 1 yr after diagnosis of MDD without treatment: 40% of individuals will still have symptoms that are sufficiently severe to meet criteria for MDD, 20% will continue to have some symptoms that no longer meet criteria for MDD, 40% will have no symptoms

PERSISTENT DEPRESSIVE DISORDER

DSM-5 DIAGNOSTIC CRITERIA FOR PERSISTENT DEPRESSIVE DISORDER
Note: in DSM-IV-TR this was referred to as Dysthymic Disorder

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A. depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for ≥2 yr
   Note: In children and adolescents, mood can be irritable and duration must be at least 1 yr
B. presence, while depressed, of ≥2 of the following
   - poor appetite or overeating
   - insomnia or hypersomnia
   - low energy or fatigue
   - low self-esteem
   - poor concentration or difficulty making decisions
   - feelings of hopelessness
C. during the 2 yr period (1 yr for children or adolescents) of the disturbance, the person has never been without the symptoms in criteria A and B for more than 2 mo at a time
D. criteria for a major depressive disorder may be continuously present for 2 yr
E. there has never been a manic episode or a hypomanic episode, and criteria have never been met for cyclothymic disorder
F. the disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder
G. the symptoms are not due to the direct physiological effects of a substance or another medical condition
H. the symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

- **specifiers**:
  - with anxious distress, mixed features, melancholic features, atypical features, mood-congruent psychotic features, mood-incongruent psychotic features, catatonia, peri-partum onset, seasonal pattern
  - partial remission, full remission
  - early onset (<21 y/o), late onset (>21 y/o)
  - with pure dysthymic syndrome (full criteria for MDE have not been met in at least preceding 2 yr), with persistent MDE (full criteria for MDE have been met throughout preceding 2 yr)
  - with intermittent MDEs, with current episode: full criteria for a MDE are currently met, but there have been periods of at least 8 wk in at least the preceding 2 yr with symptoms below the threshold for a full MDE
  - with intermittent MDEs, without current episode: full criteria for a MDE are not currently met, but there has been one or more MDEs in at least the preceding 2 yr
  - specify current severity: mild, moderate, severe

See Landmark Psychiatry Trials table for more information on TRANSFORM-2, which details the use of esketamine nasal spray for patients with treatment-resistant depression.

Epidemiology
- lifetime prevalence: 2-3%; M=F

Treatment
- psychological
  - traditionally, psychotherapy was the principal treatment for persistent depressive disorder; recent evidence suggests some (but generally inferior) benefit for pharmacological treatment. Combinations of the two may be most efficacious
- biological
  - antidepressant therapy: SSRIs (e.g. sertraline, escitalopram), TCAs (e.g. nortriptyline)

Postpartum Mood Disorders

Postpartum "Blues"
- transient period of mild depression, mood instability, anxiety, decreased concentration; considered to be normal in response to fluctuating hormonal levels, the stress of childbirth, and the increased responsibilities of motherhood
- occurs in 50-80% of mothers; begins 2-4 d postpartum, usually lasts 48 h, can last up to 10 d
- does not require psychotropic medication
- usually mild or absent: feelings of inadequacy, anhedonia, thoughts of harming baby, suicidal thoughts

MAJOR DEPRESSIVE DISORDER WITH PERIPARTUM ONSET (POSTPARTUM DEPRESSION)

Clinical Features
- this specifier can apply to a MDE with onset during pregnancy or within 4 wk following delivery
- typically lasts 2-6 mo; residual symptoms can last up to 1 yr
- may present with psychosis (rare, 0.2% – more frequent with prior post-partum mood episodes and post-partum mania)
- severe symptoms may include complete disinterest in baby, suicidal and infanticidal ideation

Epidemiology
- occurs in up to 3-6% of mothers, up to 50% risk of recurrence

Risk Factors
- previous history of a mood disorder (postpartum or otherwise), family history of mood disorder
- psychosocial factors: stressful life events, unemployment, marital conflict, lack of social support, unwanted pregnancy, colicky or sick infant

Treatment
- psychotherapy (CBT or IPT)
- short-term safety of maternal SSRIs for breastfeeding infants established; long-term effects unknown
- if depression severe or psychotic symptoms present, consider ECT

Prognosis
- impact on child development: increased risk of cognitive delay, insecure attachment, behavioural disorders
- treatment of mother improves outcome for child at 8 mo through increased mother-child interaction

Bipolar Disorders

BIPOLAR I / BIPOLAR II DISORDER

Definition
- Bipolar I Disorder
  - disorder in which at least one manic episode has occurred
  - if manic symptoms lead to hospitalization, or if there are psychotic symptoms, the diagnosis is bipolar I
  - commonly accompanied by at least 1 MDE but not required for diagnosis
  - time spent in mood episodes: 53% asymptomatic, 32% depressed, 9% cycling/mixed, 6% hypo/manic
- Bipolar II Disorder
  - disorder in which there is at least 1 MDE, 1 hypomanic episode, and no manic episodes
  - while hypomania is less severe than mania, bipolar II is not a "milder" form of bipolar I
  - time spent in mood episodes: 46% asymptomatic, 50% depressed, 1% cycling/mixed, 2% hypo/manic
  - bipolar II is often missed due to the severity and chronicity of depressive episodes and low rates of spontaneous reporting and recognition of hypomanic episodes

Selective Serotonin Reuptake Inhibitors in Pregnancy and Infant Outcomes
Paediatr Child Health 2011;16:562-63
Canadian Paediatric Society (CPS) clinical practice guideline recommendations: It is important to treat depression in pregnancy. There is no evidence that SSRIs increase the risk of major malformations. There is conflicting evidence concerning the association of paroxetine and cardiac malformations. SSRIs are not contraindicated while breast-feeding.

Antidepressant Use in Pregnancy and the Risk of Cardiac Defects
NEJM 2014 Jun 19;370(25):2397-2407
Background: It is uncertain whether selective serotonin-reuptake inhibitors (SSRIs) and other antidepressants during pregnancy are associated with increased risk of congenital cardiac defects. There are concerns about an association between paroxetine use and right ventricular outflow tract obstruction, and between sertraline use and ventricular septal defects.
Methods: Cohort study including 949504 women enrolled in Medicaid for a 7 yr period. The risk of major cardiac defects among infants born to women who took antidepressants during the 1st trimester was compared with the risk among infants born to women who did not use antidepressants. An unadjusted analysis was used, possible confounders were considered.
Results: Overall, the chance of infants not exposed to antidepressants born with a cardiac defect was 72.3 per 10000 infants, and infants with exposure was 90.1 per 10000 infants. The relative risks of any cardiac defect with the use of SSRIs were 1.06 (95% CI, 0.93 to 1.22) in the fully adjusted analysis restricted to women with depression. No significant association was found between the use of paroxetine and right ventricular outflow tract obstruction (RR, 1.07) or between the use of sertraline and ventricular septal defects (RR, 1.04).
Conclusions: No substantial increase in risk of cardiac malformations attributable to antidepressant use during the 1st trimester.

Bipolar II is quite often missed and many patients are symptomatic for up to a decade before accurate diagnosis and treatment

Patients with bipolar disorder are at higher risk for suicide when they switch from mania to depression, especially as they become aware of consequences of their behaviour during the manic episode

Classification
- classification of BD involves describing the disorder (I or II) and the current or most recent mood episode as either manic, hypomanic, or depressed
- specifiers: with anxious distress, hypo/manic/depressed with mixed features, rapid cycling, melancholic features, atypical features, mood-congruent or -incongruent psychotic features, catatonia, peripartum onset, seasonal pattern, rapid cycling (≥4 mood episodes in 1 yr)

Epidemiology
- lifetime prevalence: 1% BD I, 1.1% BD II, 2.4% Subthreshold BD; M:F = 1:1
- mean age of onset: 25 yr, usually MDE first, manic episode 6-10 yr after, average age of first manic episode: 32 yr

Risk Factors
- genetic: 60-65% of bipolar patients have family history of a major mood disorder, especially bipolar disorder
- clinical features of MDE history favouring bipolar over unipolar diagnosis: early age of onset (<25 yr), increased number of MDEs, psychotic symptoms, postpartum onset, anxiety disorders (especially separation, panic), antidepressant failure due to early "poop out" or hypomanic symptoms, early impulsivity and aggression, substance misuse, cyclothymic temperament, family history of bipolar disorder

Treatment
- lifestyle: psychoeducation regarding cycling nature of illness, ensure regular check ins, develop early warning system, "emergency plan" for manic episodes, promote stable routine (sleep, meals, exercise)
- biological: lithium, anticonvulsants, antipsychotics, ECT (if resistant); monotherapy with antidepressants should be avoided
  - mood stabilizers vary in their ability to treat (reduce symptoms acutely) or stabilize (prevent relapse and recurrence) manic and depressive symptoms; multi-agent therapy is common
  - treating mania: lithium, divalproex, carbamazepine (2nd line), SGA, ECT (2nd line), benzodiazepines (for acute agitation)
  - preventing mania: same as above but usually at lower dosages, minus ECT and benzodiazepines
  - treating depression: lithium, lurasidone, quetiapine, lamotrigine, antidepressants (2nd line, only with mood stabilizer), ECT (2nd line)
  - preventing depression: same as above plus aripiprazole, divalproex (note: quetiapine is first line in treating bipolar II depression)
  - mixed episode or rapid cycling: multi-agent therapy: lithium or divalproex + SGA (lurasidone, aripiprazole)
- psychological: supportive psychotherapy, CBT, IPT or interpersonal social rhythm therapy, family therapy
- social: vocational rehabilitation, consider leave of absence from school/work, assess capacity to manage finances, drug and EtOH cessation, sleep hygiene, social skills training, recruitment and education of family members

Course and Prognosis
- high suicide rate (15% mortality from suicide), especially depressive episodes in mixed states
- bipolar I and II disorder are chronic conditions with a relapsing and remitting course featuring alternating manic and depressive episodes; depressive symptoms tend to occur more frequently and last longer than manic symptoms
- can achieve high level of functioning between episodes
- may switch rapidly between depression and mania without any period of euthymia in between
- high recurrence rate for mania – 90% will have a subsequent episode in the next 5 yr
- long term follow-up of bipolar I – 15% well, 45% well with relapses, 30% partial remission, 10% chronically ill

CYCLOTHYMIA

Diagnosis
- presence of numerous periods of hypomanic and depressive symptoms (not meeting criteria for full hypomanic episode or MDE) for ≥2 yr; never without symptoms for >2 mo
- have never met criteria for MDE, manic or hypomanic episodes
- symptoms are not due to the direct physiological effects of a substance or GMC
- symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

Treatment
- similar to Bipolar I: mood stabilizer ± psychotherapy

Lithium is among few agents with proven efficacy in preventing suicide attempts and completions

Monotherapy with antidepressants should be avoided in patients with bipolar depression as patients can switch from depression into mania

The 4 L's for Bipolar Depression
Lithium, **L**amotrigine, **L**urasidone, Seroque**L**

A Randomized Controlled Trial of Cognitive Therapy for Bipolar Disorder: Focus on Long-Term Change
J Clin Psychiatry 2006;67:277-86
Purpose: To evaluate long-term change with cognitive therapy plus emotive techniques for the treatment of bipolar disorder.
Methods: Blinded RCT including patients with DSM-IV bipolar I or II disorder allocated to either a 6 mo trial of cognitive therapy (CT) with emotive techniques or treatment as usual. Both groups received mood stabilizers. Main outcomes were relapse rates, dysfunctional attitudes, psychosocial functioning, hopelessness, self-control, and medication adherence. Patients were assessed by independent raters blinded to treatment group.
Results: At 6 mo, CT patients experienced fewer depressive symptoms and fewer dysfunctional attitudes. There was a non-significant (p=0.06) trend to greater time to depressive relapse. At 12 mo follow-up, CT patients had lower Young Mania Rating scores and improved behavioural self-control. At 18 mo, CT patients reported less severity of illness.
Conclusions: CT appears to provide benefits in the 12 mo after completion of therapy.

Efficacy of Cognitive-Behavioural Therapy in Patients with Bipolar Disorder: A Meta-Analysis of Randomized Controlled Trials
PLoS One 2017;12(5):e0176849
Purpose: To determine the efficacy of cognitive behavioural therapy (CBT) in the treatment of type I and II bipolar disorder.
Methods: A systematic review and meta-analysis of RCTs of CBT in the treatment of adults with bipolar disorder.
Results: Nineteen RCTs including 1284 patients with type I or II BD were included. CBT lowered the relapse rate (pooled OR = 0.506; 95% CI = 0.278 −0.921) and improved depressive symptoms (g = −0.494; 95% CI = −0.963 to −0.026), mania severity (g = −0.581; 95% CI = −1.127 to −0.035), and psychosocial functioning (g = 0.457; 95% CI = 0.106–0.809). Greater effects were seen with CBT treatment duration >90 min. Relapse rates were lower in people with type I bipolar disorder.

Anxiety Disorders

Definition

- fear is a universal human experience which can serve as an adaptive mechanism to facilitate appropriate reactions to external threat
- anxiety may be seen as pathological fear when:
  - fear is greatly out of proportion to risk/severity of threat
  - response continues beyond existence of threat (prolonged, excessive, etc.) or becomes generalized to other similar or dissimilar situations
  - social or occupational functioning is impaired
- manifestations of anxiety are a result of the activation of the sympathetic nervous system and can be described through:
  - physiology: main brain structure involved is the amygdala; neurotransmitters involved include 5-HT, cholecystokinin, epinephrine, norepinephrine, and DA
  - psychology: one's thoughts about a given situation or stimulus contribute to the feeling of fear and perception of threat
  - behaviour: anxiety can lead to avoidance which can perpetuate the fear/avoidance
  - often comorbid with substance use and depression; more than 50% have multiple anxiety disorders
  - when starting medication for anxiety: start low, go slow, aim high and explain symptoms to expect prior to initiation of therapy to prevent non-adherence due to side effects
  - psychotherapy: individual or group CBT

Differential Diagnosis

Table 2. Differential Diagnosis of Anxiety Disorders

Cardiovascular	Post-MI, arrhythmia, congestive heart failure, pulmonary embolus, mitral valve prolapse
Respiratory	Asthma, COPD, pneumonia
Endocrine	Hyperthyroidism, hypoglycemia, hyperadrenalism, hyperparathyroidism
Metabolic	Vitamin B_{12} deficiency, folate deficiency, porphyria, hypoxemia, hypercalcemia
Neurologic	Neoplasm, vestibular dysfunction, encephalitis, trauma (contusion or hematoma), MS, temporal lobe epilepsy, migraine
Infectious	Cerebral (meningitis, HIV, syphilis) or systemic
GI	Gastritis, esophageal spasm
Substance-Induced	Intoxication (caffeine, cannabis, amphetamines, cocaine, thyroid replacement, OTC for colds/decongestants, steroids), withdrawal (benzodiazepines, alcohol)

Medical Workup of Anxiety Disorder

- only proceed with medical workup as clinically indicated
- routine screening: vitals, physical exam, CBC, electrolytes, thyroid function test, glucose, ECG
- additional screening: extended electrolytes, vitamin B_{12}, beta-HCG, folate, chest x-ray, any other tests as per DDx in Table 2

Risk Factors for the Development of Anxiety Disorders

- biological
  - endocrine disorders (i.e. hyperthyroidism), respiratory conditions (i.e. asthma), CNS conditions (i.e. temporal lobe epilepsy), substances/medications (i.e. excessive stimulant use), chronic medical illness
  - personal or family history of anxiety or mood disorder
  - XX>XY chromosomes
- psychological
  - current stress, early childhood adversity or trauma, early parental loss, parental factors

Panic Disorder

DSM-5 DIAGNOSTIC CRITERIA FOR PANIC DISORDER

Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 2013. American Psychiatric Association

A. recurrent unexpected panic attacks; a panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur
   - palpitations, pounding heart, or accelerated heart rate
   - sweating
   - trembling or shaking
   - sensations of shortness of breath or smothering
   - feelings of choking
   - chest pain or discomfort
   - nausea or abdominal distress
   - feeling dizzy, unsteady, light-headed, or faint
   - chills or heat sensations
   - paresthesias (numbness or tingling sensations)

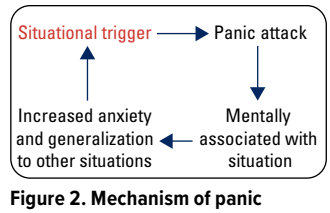

Figure 2. Mechanism of panic attacks

- derealization (feelings of unreality) or depersonalization (being detached from oneself)
- fear of losing control or "going crazy"
- fear of dying

B. at least one of the attacks has been followed by 1 mo (or more) of one or both of the following:
- persistent concern or worry about additional panic attacks or their consequences
- a significant maladaptive change in behaviour related to the attacks

C. the disturbance is not attributable to the physiological effects of a substance or another medical condition

D. the disturbance is not better explained by another mental disorder

Epidemiology
- lifetime prevalence: 5% (one of the top five most common reasons to see a family physician); M:F=1:2-3
- onset: average early-mid 20s, familial pattern
- comorbidities: depression, agoraphobia, medical comorbidity

Treatment
- pharmacological and psychological treatment together can be very effective
- psychological
  - CBT: exposure (graduated exposure to unpleasant sensations of arousal associated with a panic attack for experiential disconfirmation of their fears), cognitive restructuring (addressing underlying beliefs regarding the panic attacks), relaxation techniques (visualization, box-breathing), psychoeducation
- pharmacological (first line agents)
  - SSRIs: fluoxetine, citalopram, escitalopram, paroxetine, sertraline, fluvoxamine
  - SNRI: venlafaxine extended release
  - with SSRI/SNRIs, start with low doses and titrate up as tolerated
  - anxiety disorders often require treatment at higher doses for a longer period of time than depression (full response may take up to 12 wk)
  - treat for up to 1 yr after symptoms resolve to avoid relapse
  - explain expected adverse effects prior to initiation of therapy to prevent non-adherence
  - other antidepressants: (mirtazapine, TCAs)
  - benzodiazepines considered 2nd line (short-term, lowest effective dose, helpful while titrating antidepressant)

Prognosis
- 85% can achieve good results, 10-20% continue with significant symptoms. Longer term, 65% achieve remission
- clinical course: chronic, but episodic with psychosocial stressors

Criteria for Panic Attack (≥4)

STUDENTS FEAR the 3 Cs
Sweating
Trembling/shaking
Unsteadiness, dizziness
Depersonalization, Derealization
Excessive heart rate, palpitations
Nausea/abdominal distress
Tingling/numbness
Shortness of breath
Fear of dying, losing control, going crazy
3 Cs: **C**hest pain, **C**hills/hot flashes, **C**hoking

Duration typically 5-10 min

Panic Attack vs. Panic Disorder
- **Panic disorder** requires recurrent, unexpected panic attacks + fear of another panic attack
- **Panic attacks** can occur in the context of many different disorders

Starting Medication for Anxiety
Start low, go slow, aim high and explain symptoms to expect prior to initiation of therapy to prevent non-adherence due to side effects

Agoraphobia

DSM-5 DIAGNOSTIC CRITERIA FOR AGORAPHOBIA
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A. marked fear or anxiety about two (or more) of the following five situations:
- using public transportation
- being in open spaces
- being in enclosed places
- standing in line or being in a crowd
- being outside of the home alone

B. the individual fears or avoids these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms or other incapacitating or embarrassing symptoms

C. the agoraphobic situations almost always provoke fear or anxiety

D. the agoraphobic situations are actively avoided, require the presence of a companion, or are endured with intense fear or anxiety

E. the fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context

F. the fear, anxiety, or avoidance is persistent, typically lasting ≥6 mo

G. the fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

H. if another medical condition is present, the fear, anxiety, or avoidance is clearly excessive

I. the fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder and are not related exclusively to obsessions, perceived defects or flaws in physical appearance, reminders of traumatic events, or fear of separation

Note: agoraphobia is diagnosed irrespective of the presence of panic disorder. If an individual's presentation meets criteria for panic disorder and agoraphobia, both diagnoses should be assigned

Treatment
- as per specific panic disorder

Generalized Anxiety Disorder

DSM-5 DIAGNOSTIC CRITERIA FOR GENERALIZED ANXIETY DISORDER

Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 2013. American Psychiatric Association

A. excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 mo, about a number of events or activities (such as work or school performance)
B. the individual finds it difficult to control the worry
C. the anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 mo)
    1. restlessness or feeling keyed up or on edge
    2. being easily fatigued
    3. difficulty concentrating or mind going blank
    4. irritability
    5. muscle tension
    6. sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep)
D. the anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
E. the disturbance is not attributable to the physiological effects of a substance or another medical condition
F. the disturbance is not better explained by another mental disorder

Criteria for GAD (≥3)

C-FIRST
Concentration issues
Fatigue
Irritability
Restlessness
Sleep disturbance
Tension (muscle)

Epidemiology

- 1 yr prevalence: 1-4%, lifetime prevalence 6%; M:F=1:2
    - 8% of all who seek primary care treatment (WHO)
    - in primary care: 70% initially present with physical symptoms as main concern
- bimodal age of onset: before 20 or middle adulthood

Source: Depression and other common mental disorders: Global health estimates. Geneva: World Health Organization, 2017.

Treatment

- lifestyle: avoid caffeine and EtOH, sleep hygiene
- psychological: CBT (cognitive restructuring), muscle relaxation techniques, mindfulness
- biological
    - 1st line: SSRIs (escitalopram, sertraline, paroxetine), SNRIs (venlafaxine XR, duloxetine), pregabalin
    - benzodiazepines considered 2nd line (short-term, lowest effective dose, helpful while titrating antidepressant)
    - β-blockers not recommended

Prognosis

- good with treatment
- depends on pre-morbid personality functioning, stability of relationships, work, and severity of environmental stress

Social Anxiety

- definition: marked and persistent (>6 mo) fear of social or performance situations in which one is exposed to unfamiliar people or to possible scrutiny by others. They fear that they will be negatively evaluated in a way that may be humiliating, embarrassing, or lead to rejection (e.g. public speaking, initiating or maintaining conversation, dating, eating in public)
- situations are avoided or endured with intense anxiety and causes significant distress or impairment in functioning
- lifetime prevalence 8-12%; M:F ratio approximately equal

Phobic Disorders

Specific Phobias

- definition: marked and persistent (>6 mo) fear that is excessive or unreasonable, cued by presence or anticipation of a specific object or situation
- lifetime prevalence 10-13%; M:F ratio variable
- types: animal/insect, environment (e.g. heights, storms), blood/injection/injury, situational (e.g. airplane, closed spaces), other (e.g. loud noise, clowns), multiple fears

Diagnostic Criteria for Phobic Disorders

- marked fear/anxiety about a specific object/situation
- exposure to stimulus almost invariably provokes an immediate fear/anxiety response; may present as a panic attack
- phobic object/situation is actively avoided or endured with intense anxiety.
- fear/anxiety out of proportion to actual danger/sociocultural context and persistent (lasting 6 mo or more)
- person recognizes fear as excessive or unreasonable
- significant impact on daily routine, occupational/social functioning and/or marked distress

Treatment
- psychological: psychoeducation, CBT (focusing on both in vivo and virtual exposure therapy, gradually facing feared situations)
- biological: minimal role for medications

Obsessive-Compulsive and Related Disorders

Obsessive-Compulsive Disorder

DSM-5 DIAGNOSTIC CRITERIA FOR OBSESSIVE-COMPULSIVE DISORDER
Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 2013. American Psychiatric Association

A. presence of obsessions, compulsions, or both
   - obsessions are defined by (1) and (2)
     1. recurrent and persistent thoughts, urges, or images that are experienced, at some time during the disturbance, as intrusive and unwanted, and that in most individuals cause marked anxiety or distress
     2. the individual attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e. by performing a compulsion)
   - compulsions are defined by (1) and (2)
     1. repetitive behaviours (e.g. hand washing, ordering, checking) or mental acts (e.g. praying, counting, repeating words silently) that the individual feels driven to perform in response to an obsession or according to rules that must be applied rigidly
     2. the behaviours or mental acts are aimed at preventing or reducing anxiety or distress, or preventing some dreaded event or situation; however, these behaviours or mental acts are not connected in a realistic way with what they are designed to neutralize or prevent, or are clearly excessive

B. the obsessions or compulsions are time-consuming (e.g. take >1 h/d) or cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

C. the obsessive-compulsive symptoms are not attributable to the physiological effects

D. the disturbance is not better explained by the symptoms of another mental disorder

- **specifiers**: with good or fair insight, with poor insight, with absent insight/delusional beliefs, tic-related
- **most common obsessions**: contamination fear, pathological doubts, harm (sex, aggression), somatic dysfunctions, need for symmetry, religious
- **most common compulsions**: checking, washing, repeating, ordering, counting, need to ask, and hoarding
- rituals serve to counteract the anxiety induced by the obsessive thoughts

Epidemiology
- lifetime prevalence 3%
- mean age of onset: 20 yr; onset after 35 yr rare
- rate of OCD in first-degree relatives is higher than in the general population
- common comorbidities: anxiety disorders (>75%), depressive or bipolar disorder (>60%), obsessive-compulsive PD, tic disorders, substance use disorder, body dysmorphic disorder, trichotillomania, and excoriation disorder

Risk Factors
- etiology unknown but linked with:
  - neurological abnormalities: neurological dysfunction (brain injury, Sydenham's or Huntington's chorea), abnormal EEG, and abnormal evoked auditory potentials
  - family history of OCD or Tourette's disorder
  - paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) in children following group A β-streptococcal infection; also linked to D8/17 antigen positivity
  - social isolation, physical abuse, negative emotionality

Treatment
- CBT: ERP which involves exposure to feared situations using various techniques (e.g. imaginal exposure, systematic desensitization, flooding) with the addition of preventing the compulsive behaviours; cognitive strategies include challenging underlying beliefs
- pharmacotherapy: SSRIs (12-16 wk potential delay until response, higher therapeutic dosages than used for depression), clomipramine; adjunctive antipsychotics (risperidone, aripiprazole) for refractory OCD
- neurosurgery or neurostimulation: anterior cingulotomy for severe refractory OCD, two techniques: radiofrequency thermolesion and gamma knife capsulotomy or cingulotomy (50-70% response rate); ECT (particularly for those with comorbid severe depression)

Prognosis
- may be refractory and chronic with waxing and waning symptoms (<20% remission rate without treatment)

Related Disorders

Body Dysmorphic Disorder
- preoccupation with ≥1 perceived flaws in physical appearance not observed by others
- repetitive behaviours (e.g. mirror checking, excessive grooming, skin picking, or reassurance seeking) or mental acts (e.g. comparing self to others) related to appearance
- ± muscle dysmorphia
- causes clinically significant distress or functional impairment
- rule out eating disorder
- mean age of onset: 15 y/o
- symptoms tend to be chronic; high rate of suicidal ideation and attempts; comorbidity with MDD, social anxiety disorder, and OCD

Hoarding Disorder
- persistent difficulty discarding possessions regardless of actual value
- feels the need to save items, discarding creates distress
- results in possessions cluttering/compromising active living areas (may be uncluttered with 3rd party intervention, i.e. family member, cleaners, authorities)
- causes clinically significant distress or functional impairment
- rule out brain injury, cerebrovascular disease, Prader-Willi syndrome, OCD, MDD (low energy), psychotic disorder (delusions), neurocognitive disorder, ASD (restricted interests)
- tends to begin in teens and worsens over time, more common in older populations, large genetic component

Trichotillomania (Hair-Pulling Disorder)
- recurrent pulling out own hair resulting in hair loss (usually involves scalp, eyebrows, or eyelashes but may include other hair)
- repeated attempts to stop or decrease hair pulling
- causes clinically significant distress or functional impairment
- rule out dermatological condition, body dysmorphic disorder
- treatment: CBT (habit reversal training), SSRIs, 2nd gen. antipsychotics, N-acetylcysteine, or lithium

Excoriation (Skin-Picking) Disorder
- recurrent skin picking resulting in lesions
- repeated attempts to stop or decrease skin picking
- causes clinically significant distress or functional impairment
- rule out scabies, substance use (e.g. cocaine), psychotic disorder (e.g. delusions, tactile hallucinations), body dysmorphic disorder, stereotypic movement disorder, non-suicidal self-injury
- treatment similar to trichotillomania (described above)

Trauma- and Stressor-Related Disorders

Post-Traumatic Stress Disorder

DSM-5 DIAGNOSTIC CRITERIA FOR POST-TRAUMATIC STRESS DISORDER
Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 2013. American Psychiatric Association.

A. exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:
   1. directly experiencing the traumatic event(s)
   2. witnessing, in person, the event(s) as it occurred to others
   3. learning that the traumatic event(s) occurred to a close family member or close friend; in cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental
   4. experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g. first responders collecting human remains: police officers repeatedly exposed to details of child abuse)

B. presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:
   1. recurrent, involuntary, and intrusive distressing memories of the traumatic event(s)
   2. recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s)
   3. dissociative reactions (e.g. flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring

The Trauma Triangle
The perpetrator
The victim
The rescuer

4. intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s)
5. marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s)

C. persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:
1. avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s)
2. avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s)

D. negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. inability to remember an important aspect of the traumatic event(s)
2. persistent and exaggerated negative beliefs or expectations about oneself, others, or the world
3. persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others
4. persistent negative emotional state (e.g. fear, horror, anger, guilt, or shame)
5. markedly diminished interest or participation in significant activities
6. feelings of detachment or estrangement from others
7. persistent inability to experience positive emotions

E. marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. irritable behaviour and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects
2. reckless or self-destructive behaviour
3. hypervigilance
4. exaggerated startle response
5. problems with concentration
6. sleep disturbance (e.g. difficulty falling or staying asleep or restless sleep)

F. duration of the disturbance (criteria B, C, D, and E) is more than 1 mo

G. the disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

H. the disturbance is not attributable to the physiological effects of a substance or another medical condition

- **specifiers**:
  - with dissociative symptoms (not attributable to physiologic effects of a substance or a medical condition); this could involve either depersonalization (persistent or recurrent experiences of feeling detached from, or as if one were an outside observer of one's mental processes or body) or derealization (persistent or recurrent experiences of unreality of surroundings)
  - with delayed expression: the full diagnostic criteria are not met until 6 mo after the event

Criteria for Post-Traumatic Stress Disorder

TRAUMA
Traumatic event
Re-experience the event
Avoidance of stimuli associated with the trauma
Unable to function
More than a Month
Arousal increased
+ negative alterations in cognition and mood

Epidemiology

- lifetime prevalence in Canada is 9%; onset in mid-late 20s
- 75% have another comorbid psychiatric disorder; increased risk of suicide 2-3x
- high rates of chronic pain, sleep problems, sexual dysfunction, cognitive dysfunction
- prevalence F:M = 2:1
- most common forms of trauma: unexpected death of someone close, sexual assault, serious illness or injury to someone close, physical assault by partner or caregiver
- risk factors: severity, duration, and proximity to trauma
- differential diagnosis: bipolar disorder, borderline personality disorder, acute stress disorder (3 d-1 mo after trauma)

Treatment

- trauma therapy, CBT
  - stage 1 - safety and stabilization: emotional regulation techniques (i.e. breathing, relaxation) to help build coping skills, medications for PTSD, manage substance use
  - stage 2 - remembrance and mourning: exposure to traumatic memories and work through distorted thoughts, relational patterns, and grief
  - stage 3 - reconnection and integration: exposure therapy, etc. create a new future, new relationships, strengthen identity
- early intervention via psychological support (not de-briefing)
- psychotherapy: CBT, DBT, supportive, eye movement desensitization and reprocessing (EMDR)
- biological
  - first line: fluoxetine, paroxetine, sertraline, venlafaxine XR (50-80% response with residual symptoms is common)
  - prazosin (for treating disturbing dreams and nightmares)
  - benzodiazepines (for acute anxiety; use with extreme caution)
  - adjunctive atypical antipsychotics (risperidone, olanzapine)

Prognosis and Complications
- substance use disorder, relationship difficulties, depression, impaired social and occupational functioning disorders, personality disorders
- 50% of patients with PTSD have complete recovery within 3 mo, symptoms tend to diminish with age

Adjustment Disorder

Definition
- a diagnosis encompassing patients who have difficulty coping with a stressful life event or situation and develop acute, often transient, emotional or behavioural symptoms that resemble less severe versions of other psychiatric conditions

Acute Stress Disorder
- May be a precursor to PTSD
- Similar symptoms to PTSD
- Symptoms persist for 3d to 1 mo after exposure to a trauma

DSM-5 DIAGNOSTIC CRITERIA FOR ADJUSTMENT DISORDER
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A. the development of emotional or behavioural symptoms in response to an identifiable stressor(s) occurring within 3 mo of the onset of the stressor(s)
B. these symptoms or behaviours are clinically significant as evidenced by either of the following:
   - marked distress that is in excess of what would be expected from exposure to the stressor
   - significant impairment in social or occupational (academic) functioning
C. the stress-related disturbance does not meet criteria for another mental disorder and is not merely an exacerbation of a pre-existing mental disorder
D. the symptoms do not represent normal bereavement
E. once the stressor (or its consequences) has terminated, the symptoms do not persist for more than an additional 6 mo

- **specifiers**: with depressed mood, with anxiety, with mixed anxiety/depression, with conduct disturbance, with mixed disturbance of conduct/emotions, unspecified

Classification
- types of stressors
  - single (e.g. termination of romantic relationship)
  - multiple (e.g. marked business difficulties and marital problems)
  - recurrent (e.g. seasonal business crises)
  - continuous (e.g. living in a crime-ridden neighbourhood)
  - developmental events (e.g. going to school, leaving parental home, getting married, becoming a parent, failing to attain occupational goals, retirement)

Epidemiology
- F:M=2:1, prevalence 2-8% of the population

Treatment
- brief psychotherapy: individual or group (particularly useful for patients dealing with unique and specific medical issues; e.g. colostomy or renal dialysis groups), crisis intervention
- biological: medications can be used to treat associated symptoms (insomnia, anxiety, or depression)
  - benzodiazepines may be used for those with significant anxiety symptoms (short-term, low-dose, regular schedule)

Bereavement

Clinical Features
- bereavement is a normal psychological and emotional reaction to a significant loss, also called grief or mourning
- length and characteristics of "normal" bereavement vary between individual cultures
- normal response: protest ➔ searching and acute anguish ➔ despair and detachment ➔ reorganization
- presence of the following symptoms may indicate abnormal grief/presence of MDD:
  - guilt about things other than actions taken or not taken by the survivor at the time of death
  - thoughts of death other than the survivor feeling that they would be better off dead or should have died with the deceased person; morbid preoccupation with worthlessness
  - marked psychomotor retardation; prolonged and marked functional impairment
  - hallucinatory experiences other than hearing the voice or transiently seeing the image of the deceased person
  - dysphoria that is pervasive and independent of thoughts or triggers of the deceased; absence of mood reactivity
- after 12 mo, if patient continues to yearn/long for the deceased, experience intense sorrow/emotional pain in response to the death, remain preoccupied with the deceased or with the circumstances of their death, then may start to consider a diagnosis of "persistent complex bereavement disorder"
- if a patient meets criteria for MDD, even in the context of a loss or bereavement scenario, they are still diagnosed with MDD

Risk Factors for Poor Bereavement Outcome
- Poor social supports
- Unanticipated death or lack of preparation for death
- Highly dependent relationship with deceased
- High initial distress
- Other concurrent stresses and losses
- Death of a child
- Pre-existing psychiatric disorders, especially depression and separation anxiety

Bereavement is associated with a significant increase in morbidity and mortality acutely following the loss, with effects seen up to 1 yr after

Treatment
- support and watchful waiting should be first line, as well as education and normalization of the grief process
- screen for increased alcohol, cigarette and drug use
- normal grief should not be treated with antidepressant or anti-anxiety medications as it is important to allow the person to experience the whole mourning process to achieve resolution
- psychosocial: grief therapy (individual or group) is indicated for those needing additional support or experiencing complex grief/bereavement or significant MDD
- pharmacotherapy: if MDD present, past history of mood disorders, or severe symptoms

Loneliness is the most common symptom that continues to persist in normal bereavement and may last several years

Neurocognitive Disorders

Delirium

- see Neurology, N21

DSM-5 DIAGNOSTIC CRITERIA FOR DELIRIUM
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A. a disturbance in attention (i.e. reduced ability to direct, focus, sustain, and shift attention) and awareness (i.e. reduced orientation to the environment)
B. the disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day
C. an additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception)
D. the disturbances in criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal (e.g. coma)
E. there is evidence from the history, physical exam, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies

Clinical Features and Assessment
- common symptoms
  - disturbance of attention: distractibility, disorientation (time, place, rarely person)
  - sleep/wake disturbance (daytime sedation, nighttime agitation or wakefulness)
  - psychotic-like symptoms such as delusions, misinterpretations, illusions, and hallucinations (visual hallucinations are organic until proven otherwise)
  - affective symptoms (anxiety, fear, depression, irritability, anger, euphoria, apathy)
  - shifts in psychomotor activity (groping/picking at clothes, attempts to get out of bed when unsafe, sudden movements, sluggishness, lethargy)
- **Note**: fluctuation/major changes in all of the above over the course of the day are to be expected - so collateral history is important
- hyperactive 30% vs. hypoactive 24% vs. mixed level of activity 46%
- Folstein Mini Mental Status Exam or the Montreal Cognitive Assessment (MoCA) are helpful to assess baseline of altered mental state (i.e. score will improve as symptoms resolve)

Risk Factors
- polypharmacy particularly involving psychoactive drugs, anticholinergics, and serotonergic medications (e.g. Cogentin, Benadryl®, benzodiazepines, opioids, and corticosteroids)
- infection, dehydration, malnutrition, immobility (including use of restraints), and use of bladder catheters
- hospitalization (incidence 10-56%); frail and surgical patients are at the greatest risk
- previous delirium
- nursing home residents (incidence 60%)
- old age (especially males)
- severe illness (e.g. cancer, AIDS)
- recent anesthesia or surgery (e.g. emergency hip fracture surgery, cardiac surgery)
- brain vulnerability: pre-existing neurologic or neurocognitive disorder, substance use disorder, past psychiatric illness

Assessment/Investigations
- history: if a patient has delirium they may not be able to provide a reliable history, collateral history required; use beside clinical assessment tools such as the Confusion Assessment Method (CAM) and bedside tests to assess for attention, memory, visuospatial and executive function, and orientation
- standard bloodwork: CBC and differential, electrolytes (including Ca^{2+}, Mg^{2+}, and PO_4^{3-}), glucose, BUN, Cr, TSH/T4, LFTs, vitamin B_{12}, folate, albumin; if indicated, order blood cultures and infectious serologies (HIV, VDRL, Hep B/C)

Confusion Assessment Method (CAM) for Diagnosis of Delirium

Highly sensitive and specific method to diagnose delirium
Part 1: an assessment instrument that screens for overall cognitive impairment
Part 2: includes four features found best able to distinguish delirium from other cognitive impairments

Need (1) + (2) + (3 or 4)
(1) Acute onset and fluctuating course
(2) Inattention
(3) Disorganized thinking
(4) Altered level of consciousness - hyperactive or hypoactive

Etiology of Delirium

I WATCH DEATH
Infectious (encephalitis, meningitis, urinary tract infection, pneumonia)
Withdrawal (alcohol, barbiturates, benzodiazepines)
Acute metabolic disorder (electrolyte imbalance, hepatic or renal failure)
Trauma (head injury, postoperative)
CNS pathology (stroke, hemorrhage, tumour, seizure disorder, Parkinson's)
Hypoxia (anemia, cardiac failure, pulmonary embolus)
Deficiencies (vitamin B_{12}, folic acid, thiamine)
Endocrinopathies (thyroid, glucose, parathyroid, adrenal)
Acute vascular (shock, vasculitis, hypertensive encephalopathy)
Toxins: substance use, sedatives, opioids (especially morphine), anesthetics, anticholinergics, anticonvulsants, dopaminergic agents, steroids, insulin, glyburide, antibiotics (especially quinolones), NSAIDs
Heavy metals (arsenic, lead, mercury)

- standard imaging: CXR and CT head (indicated especially if focal neurological deficit, acute change in status, anticoagulant use, acute incontinence, gait abnormality, Hx of cancer); if indicated, abdominal x-ray for constipation and MRI head to detect or exclude subacute stroke and multifocal inflammatory lesions in patients with negative head CT
- standard urinalysis: urine dip; if indicated, urine drug screen, urine C&S
- if indicated: lumbar puncture and EEG (typical finding in delirium is generalized slowing, can also be used to rule out underlying seizures or post-ictal states as etiology)

Management

- goal is to treat the underlying causes of delirium while minimizing the physical and psychological distress to the patient
- step 1: identify and manage underlying cause
  - identify and treat underlying cause immediately
  - stop all non-essential medications
  - maintain nutrition, hydration, electrolyte balance, and monitor vitals
  - work to ensure regular bowel movements and skin care practices to prevent pressure ulcers
- step 2: optimize the environment
  - environment: quiet, well-lit, near window for cues regarding time of day
  - optimize hearing and vision; protect sleep (with medications if need be)
  - room near nursing station for closer observation; constant care if patient climbing out of bed, pulling out lines
  - family member present (or consider 1:1 sitter) for reassurance and re-orientation
  - frequent orientation: calendar, clock, reminders
  - avoid frequent changes of assigned nursing staff as well as room transfers
  - implement falls prevention strategies and enable safe mobility
  - physical restraints to maintain safety only if necessary; minimize lines and catheters
  - calm, supportive approach; therapeutic communication
- step 3: pharmacotherapy
  - low dose, high potency antipsychotics: haloperidol has the most evidence and can be given IV or IM; initiate Haldol® 0.5-1 mg IM/IV in elderly patients q1-2 h until agitation is under control for STAT or PRN situation; 0.5-2 mg PO q4-6 h - monitor for signs of EPS and QT prolongation
  - alternatives include risperidone, which is less sedating (0.25-0.5 mg PO BID; less sedating), olanzapine (more sedating, can be anticholinergic itself), quetiapine (if EPS sensitive but risk of hypotension; 6.25-50 mg PO qHS), aripiprazole (does not prolong QTc)
  - caution: all neuroleptics prolong the QT interval and decrease seizure threshold, thus increasing risk of cardiac arrhythmias and seizures, respectively; also, patients with Parkinson's disease or Lewy body dementia are particularly at high-risk of EPS
  - ECG to assess QT interval when considering treatment with an antipsychotic agent
  - benzodiazepines only used in alcohol/substance withdrawal delirium; otherwise, can worsen delirium (antipsychotics are not useful in EtOH or benzodiazepine withdrawal delirium); however, benzodiazepines should not be stopped if they are a long-standing medication or this may precipitate the delirium
  - try to minimize drugs with anticholinergic effects
  - note: antipsychotic medications are used in delirium to treat severe patient agitation, changing delirium from the hyperactive to hypoactive state; they do not treat the underlying "acute brain state" driving the delirium

Prognosis

- up to 50% 1 yr mortality rate after episode of delirium

Factors favouring psychosis over delirium

1. Auditory hallucinations that are structured and consistent
2. Personal or family history of psychosis
3. Gradual onset (unless substance induced)
4. History of a prodrome (insidious functional decline)

Factors favouring delirium over psychosis

1. Visual or tactile hallucinations
2. Acute onset
3. No previous history of psychosis
4. Sleep/wake changes
5. More global cognitive impairment
6. Recent medical illness/medication changes

Interventions for Preventing Delirium in Hospitalized Non-ICU Patients
Cochrane DB Syst Rev 2016:CD005563
Purpose: To assess effectiveness of interventions to prevent delirium in hospitalized patients in the non-ICU setting.
Methods: This study included RCTs on both pharmacological and non-pharmacological interventions for delirium in hospitalized patients in the non-ICU setting.
Results: 39 trials involving 16082 patients assessing 22 different interventions were included. Strong evidence was identified to support the use of multi-component interventions for the prevention of delirium. Multicomponent interventions include any intervention that uses non-pharmacological approaches to target multiple risk factors for delirium. Use of the Bispectral index to monitor anesthesia reduced incidence of postoperative delirium. Evidence to date does not support the use of cholinesterase inhibitors, antipsychotics, or melatonin to reduce incidence of delirium.

Major Neurocognitive Disorder (Dementia)

- see Neurology, N22

DSM-5 DIAGNOSTIC CRITERIA FOR MAJOR NEUROCOGNITIVE DISORDER

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A. evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on
   1. concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function;
      and
   2. a substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment
B. the cognitive deficits interfere with independence in everyday activities (i.e. at a minimum, requiring assistance with complex IADLs such as paying bills or managing medications)
C. the cognitive deficits do not occur exclusively in the context of a delirium
D. the cognitive deficits are not better explained by another mental disorder (e.g. major depressive disorder, schizophrenia)
   - **Note**: if deficits do not interfere (as in B) and cognitive impairments are mild-moderate (as in A.2), this is considered "mild neurocognitive disorder;" see Neurology, N21

Specify whether due to:
- Alzheimer's disease
- frontotemporal lobar degeneration
- Lewy body disease
- vascular disease
- traumatic brain injury
- normal pressure hydrocephalus
- substance/medication use
- HIV infection
- Prion disease
- Parkinson's disease
- Huntington's disease
- another medical condition (e.g. nutritional deficiency)
- multiple etiologies
- unspecified
- also specify if mild, moderate or severe; major neurocognitive disorder diagnosis requires an impairment in functioning

Epidemiology
- prevalence increases with age: 5% in patients >65 yr, 35-50% in patients >85 yr
- probability of dementia in an older person with reported memory loss is estimated to be 60%
- prevalence is increased in people with Down's syndrome and head trauma
- Alzheimer's disease comprises >50% of cases; vascular causes comprise approximately 15% of cases (other causes of dementia neurocognitive disorder – see Neurology, N22)
- disease course: insidious onset, usually leading to death within 8-10 yr of first symptoms

The 7 As of Dementia
Amnesia: loss of memory
Aphasia: loss of language ability
Apraxia: loss of ability to carry out purposeful movement
Agnosia: no longer recognizes things through the senses
Anosognosia: not knowing what one does not know
Apathy: loss of Initiative
Altered perception

Subtypes
- with or without behavioural disturbance (e.g. wandering, agitation)
- early-onset: <65 yr, late-onset: >65 yr

Assessment and Investigations (to rule out reversible vauses)
- history: consider the 7 A's of dementia, significant changes in ADLs and IADLS, medication compliance and substance use, risk factors for dementia and delirium, mood/anxiety and psychotic symptoms, screen for non-Alzheimer's dementias, assess safety and consent/capacity issues
- cognitive tests (e.g. MMSE, Rowland Universal Dementia Assessment Scale, Frontal Assessment Battery, MoCA)
- MoCA 18-25 suggestive of mild NCD, <18 suggestive of major NCD; beware of many false positives)
- standard "neurocognitive work-up": see *Delirium*, PS23
- as indicated: VDRL, HIV, LP, CXR, EEG, SPECT, head CT, or MRI
- indications for head imaging: same as for delirium, plus: age <60, rapid onset (unexplained decline in cognition or function over 1-2 mo), dementia of relatively short duration (<2 yr), recent significant head trauma, unexplained neurological symptoms (new onset of severe headache/seizures), bleeding disorder or use of anticoagulants, Hx of cancer, suspicions of normopressure hydrocephalus, and presence of unsuspected cerebrovascular disease would change management

The "Mini Cog" Rapid Assessment
3 word immediate recall
Clock drawn to "10 past 11"
3 word delayed recall

Management
- see Neurology, N22 for further management
- treat underlying medical problems and prevent new ones (e.g. treatment of hypertension and B_{12} deficiency)
- discontinue cognitively impairing medications (e.g. anticholinergic, benzodiazepines, non-benzodiazepine ("Z-drugs"))
- provide orientation cues for patient (e.g. clock, calendar)
- provide education and support for patient and family (e.g. day programs, respite care, support groups, home care)
- consider power of attorney/living will and long-term care plan (nursing home)
- inform Ministry of Transportation about patient's inability to drive safely
- consider pharmacological therapy
- to slow AD:
  - cholinesterase inhibitors (donepezil (Aricept®, 5-10 mg once daily), rivastigmine, galantamine) for mild to severe disease
  - NMDA receptor antagonist (memantine 5 mg once daily to 10 mg BID) for moderate to severe disease
- to manage AD:
  - low-dose atypical antipsychotics such as olanzapine (2.5-10 mg/d), quetiapine (25-200 mg/d), or risperidone (0.25-3 mg/d) for severe behavioural disturbances
  - trazodone (25-100 mg) can be used for night-time agitation
- to treat comorbid psychiatric conditions:
  - antidepressants such as escitalopram can be used for depressive episodes
  - "start low and go slow" (effective doses can be 1/3 to 1/2 that of regular adult age patients); reassess pharmacological therapy every 3 mo

Table 3. Comparison of Dementia, Delirium, and Cognitive Impairment Associated with Depression

	Dementia/Major Neurocognitive Disorder	Delirium	Cognitive Impairment Associated with Depression
Onset	Gradual/step-wise decline	Acute (usually hours to days)	Subacute
Duration	Months-years	Days-weeks	Variable
Natural History	Progressive Usually irreversible	Fluctuating, reversible high morbidity/mortality in the elderly	Recurrent Partially reversible
Level of Consciousness	Normal	Fluctuating between (agitation) hyperactive and stupor (hypoactive) (over 24 h)	Normal
Attention	Not initially affected	Decreased (wandering, easy distraction)	Difficulty concentrating
Orientation	Intact initially	Impaired (usually to time and place), fluctuates	Intact
Behaviour	Disinhibition, impairment in ADL/IADL, personality change, loss of social graces	Potential for agitation/retardation (even severe)	Anhedonia, decreased/increased sleep/eating, agitation/retardation
Psychomotor	Normal	Fluctuates between extremes	Slowing or agitation
Sleep Wake Cycle	Fragmented sleep at night	Reversed sleep wake cycle	Early morning awakening
Mood and Affect	Labile, anxiety or depression are common in the early stages	Anxious, irritable, fluctuating or apathetic, withdrawn	Depressed, pervasive
Cognition	Decreased executive functioning, paucity of thought	Fluctuating	May appear to be impaired/slowed
Memory Loss	Recent, eventually remote Typically, low insight	Marked recent	Recent More likely to complain
Language	Agnosia, aphasia, decreased comprehension, repetition, speech (echolalia, palilalia)	Dysnomia, dysgraphia, speech rambling, irrelevant, incoherent, subject changes	Not affected
Delusions	Compensatory	Nightmarish and poorly formed	Nihilistic, somatic
Hallucinations	Variable	Visual common	Less common; if present, auditory predominates
Quality of Hallucinations	Vacuous/bland	Frightening/bizarre	Self-deprecatory
Medical Status	Variable	Acute illness, drug toxicity	Rule out systemic illness, medications

Most Common Causes of Dementia

- **Alzheimer's disease (up to 50-60%):** predominantly memory and learning issues, insidious onset/gradual progression
- **Frontotemporal degeneration (5%):** language type (early preservation), behavioural type (apathy/disinhibition/self-neglect); more common among those with dementia that has onset before age 65; progressive
- **Lewy body disease (up to 25%):** early changes in executive and attention, may fluctuate, well-formed visual hallucinations (e.g. rabbits), autonomic impairment (falls, hypotension), Parkinson's type EPS that does not respond well to pharmacotherapy and follows >1 yr after cognitive decline, fluctuating degree of cognitive impairment, sleep disturbances
- **Vascular disease (15-30%):** vascular risk factors, focal neurological signs, abrupt onset, stepwise progression, executive dysfunction > memory impairment, personality and mood changes (loss of motivation)
- **Normal pressure hydrocephalus:** abnormal gait ("magnetic gait"), early incontinence, rapidly progressive; dilated ventricles on imaging

Substance-Related and Addictive Disorders

Overview

- substance use disorder (SUD): a neurobiological disorder involving compulsive drug seeking and drug taking, despite adverse consequences, with loss of control over drug use (think issues with the "3 Cs": compulsive, consequences, control)
- it is possible to have a substance use disorder without physiological dependence (i.e. withdrawal syndrome or tolerance), dependence is the hallmark of substance use disorders and comes in the following forms:
  - behavioural: substance-seeking activities and pathological use patterns
  - physical: physiologic withdrawal effects without use or tolerance
  - cognitive: continuous or intermittent cravings for the substance to avoid dysphoria or to attain drug state
- drug misuse: drug use that deviates from the approved social or medical pattern, usually causing impairment or disruption to function in self or others
- these disorders are usually chronic with a relapsing and remitting course
- there are 10 separate classes of substances identified in the DSM-5: alcohol; caffeine; cannabis hallucinogens (PCP or similarly acting arylcyclohexylamines, and other hallucinogens); inhalants; opioids; sedatives, hypnotics, and anxiolytics; stimulants (amphetamine-type substances, cocaine, and other stimulants); tobacco; and other (or unknown) substances
- whereas substance use disorders imply addiction to substances, addictive disorders include process (behavioural) addictions such as gambling

Epidemiology

- the lifetime prevalence of SUD in Canada is 21.6% lifetime and 10.1 % for the last 12 mo; for alcohol use disorder it is 18.1% and 3.2%; for cannabis use disorder 6.8% and 1.3% and for other substances, 4.0% and 0.7%, respectively
- 47% of those with substance use disorder have mental health problems
- 29% of those with a mental health disorder have a substance use disorder
- 47% of those with schizophrenia and 25% of those with an anxiety disorder have a substance use disorder

Etiology

- almost all drugs (and activities) related to dependence increase dopamine in the nucleus accumbens, an action that contributes to their euphoric properties and, with repeated use, to their ability to change signaling pathways in the brain's reward system
- substance use disorders arise from multifactorial interactions between genes (personality, neurobiology) and environment (low socioeconomic status, substance-using peers, adverse childhood or traumatic experiences, social isolation, systemic racism, and chronic stress)
- certain comorbid conditions may also predispose individuals to a substance use disorder (e.g. mental illness, chronic disease, acute and chronic pain)
- environmental factors play a significant role in the exposure to the substance. For instance, the over prescription of opioids for pain in North America played a major role in the development of the opioid use disorder crisis

Diagnosis

- each specific substance is addressed as a separate use disorder and diagnosed utilizing the same overarching criteria (e.g. a single patient may have moderate alcohol use disorder, and a mild stimulant use disorder)
- testing for illicit drugs is most commonly done on urine or blood samples
  - serum toxicology screen measures recent alcohol consumption but has no relation to the diagnosis of alcohol use disorder
  - toxicology may be helpful in differentiating withdrawal from other mental disorders
  - urine drug screens are useful for detecting recent drug use, but not for diagnosing drug use disorders
- substance use disorders are measured on a continuum from mild to severe based on the number of criteria met within 12 mo
  - mild: 2-3
  - moderate: 4-5
  - severe: 6 or more
- criteria for substance use disorders (**PEC WITH MCAT**)
  - use despite **P**hysical or psychological problem (e.g. alcoholic liver disease or cocaine related nasal problems)
  - failure to fulfill **E**xternal roles at work/school/home
  - **C**raving or a strong desire to use substance
  - **W**ithdrawal
  - continued use despite **I**nterpersonal problems
  - **T**olerance: needing to use more substance to get same effect
  - use in physically **H**azardous situations
  - **M**ore substance used or for longer period than intended
  - unsuccessful attempts to **C**ut down
  - **A**ctivities given up due to substance
  - excessive **T**ime spent on using or finding substance

Table 4. Substance Symptomatology

	Drugs	Symptoms of Intoxication	Symptoms of Withdrawal
CNS Depressants	Alcohol, opioids, barbiturates, benzodiazepines, GHB	Euphoria, slurred speech, disinhibition, confusion, poor coordination, coma (severe)	Anxiety, anhedonia, tremor, seizures, insomnia, psychosis, delirium, death
Stimulants	Amphetamines, methylphenidate, MDMA, cocaine	Euphoria, mania, psychomotor agitation, anxiety, psychosis (especially paranoia), insomnia, cardiovascular complications (stroke, MI, arrhythmias), seizure	'Crash', craving, dysphoria, suicidality
Hallucinogens	LSD, mescaline, psilocybin, PCP, ketamine, ibogaine, salvia	Distortion of sensory stimuli and enhancement of feelings, psychosis (++ visual hallucinations), delirium, anxiety (panic), poor coordination	Usually absent

Questions to Characterize Substance Use and Risk Assessment (THE WATER)

- When was the last **T**ime you used?
- **H**ow long can you go without using?
- Have you **E**xperienced medical or legal consequences of your use?
- Any previous attempts to cut down or quit, and did you experience any **W**ithdrawal symptoms?
- How has your substance use **A**ffected your work, school, relationships?
- Are there any **T**riggers that you know will cause you to use?
- Substances can be very **E**xpensive, how do you support your drug use?
- By what **R**oute (oral ingestion, inhalation (snorting), smoking, IV) do you usually use?

General Approach to Assessment

- a comprehensive evaluation should inquire about drug history including names of substances used, amount, frequency, duration, routes, last use, injection drug use, needle sharing, symptoms of withdrawal, consequences of use (medical, social, or personal), previous treatment programs and medical (e.g. HIV, Hepatitis B and C, chronic pain), psychiatric (e.g. mood and anxiety disorders), and social history (e.g. family and housing arrangements, any child safety concerns)
- ask about more socially accepted substances (e.g. nicotine, alcohol) before asking about use of cannabis, misuse of prescription medicines, and about illicit drugs
- obtaining collateral history is recommended as well as evaluating patient insight into the problem

Lab Testing
- urine, saliva, sweat, and hair can be tested for the presence of drugs
- urine is most commonly used due to ease of collection and adequate sensitivity and specificity, but it does not reflect serum concentrations
- proper urine drug testing involves an initial screening test (qualitative) followed by confirmatory testing for substances with positive screening results
- most confirmatory tests use gas or high-performance liquid chromatography
- post-ingestion window of detection with urine test: alcohol (7-12 h), amphetamine (48 h), barbiturates (1-21 d), short-acting benzodiazepine (72 h), long-acting benzodiazepine (30 d), cocaine (12-72 h), morphine (48-72 h), methadone (72 h), Oxycodone (2-4 d), PCP (8 d), cannabis (3 d for single use to >30 d for heavy users)
- limitations: negative tests cannot rule out substance use, and positive results cannot determine how much or frequency of use

General Approach to Treatment
- approach must be appropriate to the patient's current state of change (see Public Health and Preventive Medicine, *Health Promotion Strategies*, PH11)
- patients will only change when the pain of change appears less than the pain of staying the same
- provider can help by providing psychoeducation (emphasize neurobiologic model of addiction), motivation, and hope
- principles of motivational interviewing (see *Psychotherapy*, PS50)
  - non-judgmental stance
  - space for patient to talk and reflect
  - offer accurate empathic reflections back to patient to help frame issue
- encourage and offer referral to evidence based services
  - social: 12-step programs (alcoholics anonymous, narcotics anonymous), family education, and support
  - psychological therapy: addiction counselling, MET, CBT, contingency management, group therapy, family therapy, marital counselling
  - medical management (differs depending on substance): acute detoxification, pharmacologic agents to aid maintenance
- harm reduction whenever possible: safe-sex practices, avoid driving while intoxicated, avoid substances with child care, safe needle practices/exchange, pill-testing kits, reducing tobacco use
- comorbid psychiatric conditions: many will resolve with successful treatment of the substance use disorder but patients who meet full criteria for another disorder should be treated for that disorder with psychological and pharmacologic therapies
- always consider duty to inform Ministry of Transportation for risk of driving or operating other vehicles

Nicotine

- see Family Medicine, FM13

Alcohol

- see Family Medicine, FM15 and Emergency Medicine, ER54

History
- Validated screening questionnaire for alcohol use disorders
  - **C** ever felt the need to **C**ut down on your drinking?
  - **A** ever felt **A**nnoyed at criticism of your drinking?
  - **G** ever feel **G**uilty about your drinking?
  - **E** ever need a drink first thing in the morning (**E**ye opener)?
    - for men, a score of ≥2 is a positive screen; for women, a score of ≥1 is a positive screen
    - if positive CAGE, then assess further to distinguish between problem drinking and alcohol use disorder

Canada's Low-Risk Alcohol Drinking Guidelines

Moderate Drinking		
Men: 3 or less/d (≤15/wk)	Women: 2 or less/d (≤10/wk)	Elderly: 1 or less/d

Biochemical Markers of Prolonged Alcohol Use
- elevated liver function tests (AST, ALT, GGT), MCV, and carbohydrate-deficient transferrin (CDT)
- AST:ALT ratio >2:1 and elevated GGT are suggestive of alcohol use

Confabulations: the fabrication of imaginary experiences to compensate for memory loss

Make sure to ask about other alcohols: mouthwash, rubbing alcohol, methanol, ethylene glycol, aftershave (may be used as a cheaper alternative)

A "Standard Drink" (SD)
Spirit (40%): 1.5 oz. or 43 mL
Table Wine (12%): 5 oz. or 142 mL
Fortified Wine (18%): 3 oz. or 85 mL
Regular Beer (5%): 12 oz. or 341 mL
OR
1 pint of beer = 1.5 SD
1 bottle of wine = 5 SD
1 "mickey" = 8 SD (375 mL)
"26-er" = 17 SD (750 mL)
"40 oz." = 27 SD

Alcohol Intoxication
- throughout Canada, the legal limit for impaired driving is a BAC ≥0.08% (≥80 mg/dL or 17.4 mmol/L) which is typically reached after 4 drinks in women and 5 drinks in men in a 2 h period
- most signs of intoxication are present at over >21.7 mmol/L (100 mg/dL): altered perception, impaired judgement, ataxia, hyper-reflexia, impaired coordination, changes in mood/personality, prolonged reaction time, and slurred speech
- respiratory depression and arrest can occur with >60 mmol/L (non-tolerant drinkers) and 90-120 mmol/L (tolerant drinkers)

Management of Alcohol Intoxication
- stabilize patient if there is reduced level of consciousness or vomiting; assess airways and respiratory function
- administer IV crystalloid fluids if evidence of volume depletion or shock; correct electrolytes and hypoglycemia
- monitor for signs of alcohol withdrawal following detoxification in patients with alcohol use disorder

Alcohol Withdrawal
- medical emergency: occurs within 12-48 h after prolonged heavy drinking and can be life-threatening
- ~50% of middle-class, functional individuals with alcohol use disorder have experienced alcohol withdrawal; 80% in hospitalized/homeless individuals
  - alcohol withdrawal can be described as having 4 stages, however not all stages may be experienced:
    - stage 1 (onset 4-12 h after last drink): "the shakes" tremor, sweating, agitation, anorexia, cramps, diarrhea, sleep disturbance, anxiety, insomnia, headache
    - stage 2 (onset 12-24 h): alcoholic hallucinosis: visual, auditory, olfactory, or tactile hallucinations
    - stage 3 (onset 12-48 h): alcohol withdrawal seizures, usually tonic-clonic, non-focal, and brief (can occur as early as 2 h after alcohol consumption)
    - stage 4 (onset 48-96 h): delirium tremens, confusion/disorientation, delusions, hallucinations, agitation, tremors, autonomic hyperactivity (diaphoresis, fever, tachycardia, HTN)
- course: almost completely reversible in young; elderly often left with cognitive deficits
- mortality rate 20% if untreated

Management of Alcohol Withdrawal
- monitor using the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-A) scoring system
  - areas of assessment include (**SHANT AS TAV**):
    - physical (5): paroxysmal **S**weats, **H**eadache/fullness in head, **A**gitation, **N**ausea and vomiting, **T**remor
    - psychological/cognitive (2): **A**nxiety, orientation/clouding of **S**ensorium
    - perceptual (3): **T**actile disturbances, Auditory disturbances, **V**isual disturbances
    - all categories are scored from 0-7 (except: orientation/sensorium 0-4), maximum score of 67
    - mild <10, moderate 10-20, severe >20
- check for signs of hepatic failure (e.g. ascites, jaundice, and coagulopathy)

Delirium Tremens (alcohol withdrawal delirium)
- Autonomic hyperactivity (diaphoresis, tachycardia, increased respiration)
- Hand tremor
- Insomnia
- Psychomotor agitation
- Anxiety
- Nausea or vomiting
- Tonic-clonic seizures
- Visual/tactile/auditory hallucinations
- Persecutory delusions

Table 5. CIWA-A Scale Treatment Protocol for Alcohol Withdrawal

Basic protocol	Diazepam 20 mg PO q1-2 h PRN until CIWA-A <10 points
	Observe 1-2 h after last dose and re-assess on CIWA-A scale
	Thiamine 100-250 mg IM then 100 mg PO once daily for 3 d, folic acid
	Supportive care (hydration, nutrition, and electrolyte replacement)
History of withdrawal seizures	Diazepam 20 mg PO q1 h for minimum of three doses regardless of subsequent CIWA scores
If age >65 or patient has severe liver disease, severe asthma or respiratory failure	Use a short acting benzodiazepine
	Lorazepam 1-4 mg PO/SL/IM q1-2 h
If hallucinations are present	Haloperidol 2-5 mg IM/PO q1-4 h – max 5 doses/d or atypical antipsychotics (olanzapine, risperidone)
	Diazepam 20 mg x 3 doses as seizure prophylaxis (haloperidol lowers seizure threshold)
Admit to hospital if	Still in withdrawal after >80 mg of diazepam
	Delirium tremens, recurrent arrhythmias, or multiple seizures
	Medically ill or unsafe to discharge home

Wernicke-Korsakoff Syndrome
- alcohol-induced amnestic disorders due to thiamine deficiency (poor nutrition or malabsorption)
- necrotic lesions: mammillary bodies, thalamus, brainstem
- Wernicke's encephalopathy (acute and reversible): triad of oculomotor dysfunction such as nystagmus (CN VI palsy (eye pointing inwards)), gait ataxia, and confusion. If untreated, may progress to Korsakoff's syndrome
- Korsakoff's syndrome (chronic and only 20% reversible with treatment): anterograde amnesia and compensatory confabulation; cannot occur only during an acute delirium or dementia and must persist beyond usual duration of intoxication/withdrawal
- management
  - Wernicke's preventative treatment (any patient in withdrawal): thiamine 100-250 mg IM/IV x 1 dose
  - Wernicke's acute treatment: thiamine 500 mg IV BID/TID x 72 h, then reassess
  - Korsakoff's: IV treatment as for Wernicke's followed by thiamine 100 mg PO TID x 3-12 mo

Treatment of Alcohol Use Disorder
- non-pharmacological
  - see *General Approach to Treatment*, PS28
- pharmacological
  - naltrexone (Revia®): opioid antagonist, shown to be successful in reducing the "high" associated with alcohol, moderately effective in reducing cravings, frequency or intensity of alcohol binges; can be started if still consuming alcohol or abstinent but can precipitate withdrawal in those with physical opioid dependence
  - acamprosate (Campral®): NMDA glutamate receptor antagonist; useful in maintaining abstinence and decreasing cravings
  - disulfiram (Antabuse®): prevents oxidation of alcohol (blocks acetaldehyde dehydrogenase) and causes an adverse reaction to alcohol (nausea/vomiting, tachycardia, shortness of breath, headache); if patient relapses, must wait 48 h before restarting Antabuse®; prescribed only when treatment goal is abstinence; RCT evidence is generally poor or negative due to poor medication adherence; contraindicated in severe renal disease, pregnancy, psychoses, and cardiac disease
  - some evidence for the use of gabapentin, topiramate, and ondansetron as anti-craving agents, but not approved by Health Canada approved for this indication (currently under investigation)

Opioids

- types of opioids: heroin, morphine, oxycodone, Tylenol #3® (codeine), hydromorphone, fentanyl, methadone, meperidine (Demerol®)
- in addition to working on opiate receptors, opiates also act on the dopaminergic system, which mediates their addictive properties
- most commonly used are: Percocet® (oxycodone/acetaminophen), Vicodin® (hydrocodone/acetaminophen), and OxyContin® (oxycodone)
- major risks associated with the use of contaminated needles: increased risk of hepatitis B and C, bacterial endocarditis, and HIV/AIDS
- recent considerations of inadvertent overdose secondary to contamination with fentanyl in the drug supply "opioid crisis" leading to 9000 deaths in Canada between January 2016 and June 2018

Acute Intoxication
- direct effect on receptors in CNS resulting in decreased pain perception, sedation, decreased sex drive, nausea/vomiting, decreased GI motility (constipation and anorexia), pupil constriction (e.g. pinpoint pupils; exception is meperidine), and respiratory depression (can be fatal)
- medical emergency: typical syndrome includes shallow respirations, miosis, bradycardia, hypothermia, decreased level of consciousness
- management
  - ABCs
  - IV glucose
  - naloxone hydrochloride (Narcan®): 0.4 mg up to 2 mg IV for diagnosis
  - treatment: intubation and mechanical ventilation, ± naloxone drip, until patient alert without naloxone (up to >48 h with long-acting opioids)
- caution: opioids have a longer half-life than naloxone; may need to observe for toxic reaction for at least ≥24 h

Withdrawal
- symptoms: dysphoric mood, insomnia, drug-craving, myalgias, nausea or vomiting, yawning, chills, lacrimation, rhinorrhea, pupillary dilation, piloerection, sweating, diarrhea, fever; withdrawal symptoms can be severe but are not life threatening
- onset: 6-12 h (depending on half-life of opioid used); duration: 5-10 d
- complications: loss of tolerance (overdose on relapse), miscarriage, premature labour
- management: long-acting oral opioids (methadone, buprenorphine), α-adrenergic agonists (clonidine for symptomatic management of autonomic signs and symptoms of withdrawal)
- monitor withdrawal severity using Clinical Opioid Withdrawal Scale (COWS)

Opioid Antagonists
Naltrexone vs. Naloxone
Naltrexone (Revia®)
- Can be used for EtOH dependence (although not routinely used)
- Long half life (h)

Naloxone (Narcan®)
- Used for life-threatening CNS/respiratory depression in opioid overdose
- Short half life (<1 h)
- Very fast acting (min)
- High affinity for opioid receptor
- Induces opioid withdrawal symptoms

Maintenance Medication for Opiate Addiction: The Foundation of Recovery
J Addict Dis 2012;31:207-225
Maintenance treatment of opioid addiction with methadone or buprenorphine is associated with retention in treatment, reduction in illicit opiate use, decreased craving, and improved social function. Recently, studies showing extended release naltrexone injections have showed some promise.

Classic Opioid Overdose Triad (RAM)
Respiratory Depression
Altered Mental Status
Miosis

Treatment of Opioid Use Disorder

- see *General Approach to Treatment*, PS28
- long-term treatment may include maintenance treatment with methadone (opioid agonist) or buprenorphine (mixed agonist-antagonist)
- caution: methadone can cause QTc interval prolongation, screening ECG recommended
- Suboxone® formulation includes naloxone in addition to buprenorphine, in an effort to prevent injection of the drug. When naloxone is injected, it will precipitate opiate withdrawal and block the opiate effect of buprenorphine. However, it will not have this antagonist action when taken sublingually
- decreasing risk of overdose: patients with opiate use disorder should be encouraged to carry a naloxone kit and educated on ways to limit overdose risk (i.e. use with a friend, avoid mixing drugs)

Cocaine

- street names: blow, C, coke, crack, flake, freebase, rock, snow
- alkaloid extracted from leaves of the coca plant; blocks presynaptic uptake of serotonin (causing euphoria), dopamine (linked to its addictive effect), norepinephrine and epinephrine (causing vasospasm, HTN)
- sodium channel blockade: cocaine slows or blocks nerve conduction and acts as a local anesthetic by altering recovery of neuronal Na^+ channels; it has a similar effect on cardiac Na^+ channels and in overdose can manifest on ECG as prolongation of the QRS complex
- self-administered by inhalation/smoking (crack) (90% bioavailability), insufflation (i.e. intranasal; 80% bioavailability), or intravenous route
- onset and duration of action: onset within seconds if inhaled or IV, lasting 15-30 min; onset in 3-5 min if insufflated, blood levels peak at 10-20 min with effects beginning to fade after 45-60 min; cocaine has a biologic half-life of 1 h, thus repeated self-administration is common among users to maintain an effect

Intoxication

- elation, euphoria, pressured speech, restlessness, sympathetic stimulation (e.g. tachycardia, mydriasis, sweating, hypertension)
- prolonged use may result in paranoia and psychosis (including tactile hallucinations)

Overdose

- medical emergency: HTN, tachycardia, tonic-clonic seizures, dyspnea, hyperthermia, and ventricular arrhythmias
- the vasoconstrictive effects of cocaine can also result in stroke, MI, or intracranial hemorrhage
- treatment with IV diazepam to control seizures
- benzodiazepines may also be used for management of moderate agitation and anxiety, whereas severe agitation may require antipsychotics
- beta-blockers (incl. labetalol or propranolol) are not recommended because of risk from unopposed alpha-adrenergic stimulation

Withdrawal

- initial "crash" (1-48 h): increased sleep, increased appetite, dysphoria (non-life threatening)
- withdrawal (1-10 wk): dysphoric mood plus fatigue, irritability, vivid unpleasant dreams, insomnia or hypersomnia, psychomotor agitation or retardation
- complications: relapse, suicide (significant increase in suicide during withdrawal period)
- management: supportive management

Treatment of Cocaine Use Disorder

- see *General Approach to Treatment*, PS28
- no pharmacologic agents have widespread evidence or acceptance of use (some evidence for off-label use of topiramate)
- referral to psychological interventions (e.g. relapse prevention) is the mainstay of long-term treatment

Complications

- cardiovascular: arrhythmias, MI, cerebrovascular accident, ruptured AAA, chest pain (accounts for 40% of all cocaine-related ED visits)
- neurologic: seizures
- psychiatric: psychosis, delirium, suicidal ideation
- other: nasal septal deterioration, acute/chronic lung injury "crack lung," possible increased risk of connective tissue disease

Common Presentations of Drug Use

System	Findings
General	Weight loss (especially with chronic use of cocaine, heroin) Injected conjunctiva (cannabis) Pinpoint pupils (opioids) Track marks (injection drugs)
MSK	Trauma
GI	Viral hepatitis (injection drugs) Unexplained elevations in ALT (injection drugs)
Behavioural	Missed appointments Non-compliance Drug-seeking (especially benzodiazepines, opioids)
Psychological	Insomnia Fatigue Depression Flat affect (benzodiazepines, barbiturates) Paranoia (cocaine) Psychosis (cocaine, cannabis, hallucinogens)
Social	Marital discord Family violence Work/school Absenteeism and poor performance

Amphetamines

- includes prescription medications for ADHD e.g. Ritalin® and Adderall® and street drugs such as crystal meth
- intoxication characterized by euphoria, improved concentration, sympathetic and behavioural hyperactivity, and at high doses. Can mimic symptoms of psychosis or mania; can eventually cause coma
- chronic use can produce psychosis which can resemble schizophrenia with agitation, paranoia, delusions, and hallucinations
- withdrawal symptoms include dysphoria, fatigue, and restlessness
- treatment of amphetamine induced psychosis: antipsychotics for acute presentation, benzodiazepines for agitation, β-blockers for tachycardia, HTN

Cannabis

- psychoactive substance: delta-9-tetrahydrocannabinol (Δ9-THC)
- general clinical manifestations: intoxication characterized by tachycardia, conjunctival vascular engorgement, dry mouth, altered sensorium, increased appetite, and muscle relaxation
- neuropsychiatric effects:
  - altered mood, perception, and thought content: increased sense of well-being, euphoria/laughter
  - impaired cognitive and psychomotor performance: reduced reaction time, impaired attention, concentration, and short-term memory. It may also impair motor coordination required to complete complex tasks requiring divided attention. Notably, psychomotor impairments may interfere with one's ability to operate heavy machinery such as automobiles
- inhaled cannabis: onset of psychoactive effects occurs rapidly with peak effects felt 15-30 min after intake and lasting up to 4 h
  - acute exacerbation in patients with asthma may be a complication with inhalation
- ingested cannabis: following oral ingestion, psychotropic effects set in with a delay of 30-90 min, reach their maximum after 2-3 h and last for about 4-12 h depending on dose
- high doses can cause depersonalization, paranoia, anxiety and may trigger psychosis and schizophrenia if predisposed
- chronic use is associated with tolerance and an apathetic, amotivational state; may also exacerbate respiratory problems such as asthma and chronic bronchitis
- assessment: standard urine drug screens
- treatment of cannabis use disorder: see *General Approach to Treatment*, PS28
- cessation following heavy use produces a significant withdrawal syndrome: irritability, anxiety, insomnia, decreased food intake

Hallucinogens

- types of hallucinogens by primary action
  - 5-HT2A agonists: LSD, mescaline (peyote), psilocybin mushrooms, DMT (ayahuasca)
  - NMDA antagonists: PCP, ketamine
  - κ-opioid agonists: salvia divinorum, ibogaine
- 5-HT2A agonists are most commonly used; intoxication characterized by tachycardia, HTN, mydriasis, tremor, hyperpyrexia, and a variety of perceptual, mood and cognitive changes (rarely, if ever, deadly; treat vitals symptomatically)
- psychological effects of high doses: depersonalization, derealization, paranoia, and anxiety (panic with agoraphobia)
- tolerance develops rapidly (hours-days) to most hallucinogens so physical dependency is virtually impossible, although psychological dependency and harmful use patterns can still occur
- no specific withdrawal syndrome characterized but may experience "flashbacks"
- management of acute intoxication: support, reassurance, diminished stimulation; benzodiazepines (e.g. lorazepam) or high potency antipsychotics (e.g. haloperidol) seldom required (if used, use small doses), minimize use of restraints
- long term adverse effects: controversial role in triggering psychiatric disorders, particularly mood or psychosis, thought to be chiefly in individuals with genetic or other risk factors
- Hallucinogen Persisting Perception Disorder: DSM-5 diagnosis characterized by long lasting, spontaneous, intermittent recurrences of visual perceptual changes reminiscent of those experienced with hallucinogen exposure

Cannabinoid Hyperemesis Syndrome
An interesting and relatively new clinical phenomenon associated with chronic cannabis use characterized by cyclical, recurrent severe nausea, vomiting, and colicky pain. Possibly due to increased potency of available THC products. Patients often present to ED in acute distress with no evidence of specific GI pathology. Many patients will successfully self-medicate with hot baths or showers

Medical Uses of Cannabis
- Chemotherapy-induced nausea and vomiting
- Spasticity, muscle spasms (multiple sclerosis, spinal cord injury)
- Chronic pain (neuropathic pain)

Cannabis Use and Risk of Psychotic or Affective Mental Health Outcomes: A Systematic Review
The Lancet 2007;370:319-28
Purpose: To review the evidence for cannabis use and occurrence of psychotic or affective mental health outcomes.
Study Characteristics: A meta-analysis of 35 population-based longitudinal studies, or case-control studies nested within longitudinal designs.
Results: There was an increased risk of any psychotic outcome in individuals who had ever used cannabis (pooled adjusted odds ratio =1.41, 95% CI 1.20-1.65). Findings were consistent with a dose-response effect, with greater risk in people who used cannabis more frequently (2.09, 95% CI, 1.54-2.84). Findings for depression, suicidal thoughts, and anxiety outcomes were less consistent. In both cases (psychotic and affective outcomes), a substantial confounding effect was present.
Conclusions: The findings are consistent with the view that cannabis increases risk of psychotic outcomes independent of transient intoxication effects, although evidence is less strong for affective outcomes. Although cannabis use and the development of psychosis are strongly associated, it is difficult to determine causality and it is possible that the association results from confounding factors or bias. The authors did conclude that there is sufficient evidence to warn young people that using cannabis could increase their risk of developing a psychotic illness later in life.

Cannabis Use and Psychosis: A Review of Reviews
Eur Arch Psychiatry Clin Neurosci 2019;10.1007/s00406-019-01068-z
Purpose: To review the evidence on cannabis use and the development of psychosis
Methods: This study included systematic reviews and meta-analyses published after 2006. Studies on cannabis use and psychosis were included regardless of use pattern (lifetime, past year, past month, daily use, intensive use, occasional use) and type of psychosis (acute psychosis, psychotic disorders, schizophrenia).
Results: 26 systematic reviews and meta-analyses met inclusion criteria. A dose dependent relationship was identified between cannabis use and the development of psychotic illness. Cannabis users also had earlier symptom onset, increased relapse rate, more hospitalization, and more positive symptoms compared to non-users.

"Club Drugs"

Table 6. The Mechanism and Effects of Common "Club Drugs"

Drug	Mechanism	Effect	Adverse Effects
MDMA ("Ecstasy", "X", "E", "M", "Molly")	Acts on serotonergic and dopaminergic pathways, properties of a hallucinogen and stimulant	Enhanced sensorium; feelings of well-being, empathy	Diaphoresis, tachycardia, fatigue, muscle spasms (especially jaw clenching), ataxia, hyperthermia, arrhythmias, DIC, rhabdomyolysis, renal failure, seizures, death
Gamma Hydroxybutyrate (GHB, "G", "Liquid Ecstasy")	Biphasic dopamine response (inhibition then release) and releases opiate-like substance	Euphoric effects, increased aggression, impaired judgment	Diaphoresis, tachycardia, fatigue, muscle spasms (especially jaw clenching), ataxia Severe withdrawal from abrupt cessation of high doses results in tremor, seizures, psychosis
Flunitrazepam (Rohypnol®, "Roofies", "Rope", "The Forget Pill")	Potent benzodiazepine, rapid oral absorption	Sedation, psychomotor impairment, amnestic effects, decreased sexual inhibition	CNS depression with EtOH
Ketamine ("Special K", "Kit-Kat")	NMDA receptor antagonist, rapid-acting general anesthetic used in paediatrics and by veterinarians	"Dissociative" state, profound amnesia/analgesia, hallucinations and sympathomimetic effects	Psychological distress, accidents due to intensity of experience and lack of bodily control In overdose: decreased LOC, respiratory depression, catatonia
Methamphetamine ("speed", "meth", "chalk", "ice", "crystal")	Amphetamine stimulant, induces norepinephrine, dopamine, and serotonin release	Rush begins in min, effects last 6-8 h, increased activity, decreased appetite, general sense of well-being, tolerance occurs quickly, users often binge and crash	Short-term use: high agitation, rage, violent behaviour, occasionally hyperthermia and convulsions Long-term use: addiction, anxiety, confusion, insomnia, paranoia, auditory and tactile hallucinations (especially formication), delusions, mood disturbance, suicidal and homicidal thoughts, stroke May be contaminated with lead, and IV users may present with acute lead poisoning
Phencyclidine ("PCP", "angel dust")	Not understood, used by veterinarians to immobilize large animals	Amnestic, euphoric, hallucinatory state	Horizontal/vertical nystagmus, myoclonus, ataxia, autonomic instability (treat with diazepam IV), prolonged agitated psychosis (treat with haloperidol) High-risk for suicide; violence towards others High dose can cause coma

Date Rape Drugs
- GHB
- Flunitrazepam (Rohypnol®)
- Ketamine (sometimes used as it is tasteless and odourless)

Formication
Tactile hallucination that insects or snakes are crawling over or under the skin (especially associated with crystal meth use but also observed among some cocaine and PCP users)

Emerging Medical Uses of Hallucinogens
Many hallucinogens are currently under investigation for therapeutic benefit; LSD & psilocybin for end of life anxiety, MDMA for PTSD, ketamine for rapid treatment of depression, ibogaine derivatives for addiction

Malingering: intentional production of false or grossly exaggerated physical or psychological symptoms, motivated by secondary gain/external reward (e.g. avoiding work, obtaining financial compensation, or obtaining drugs)

Factitious Disorder: intentional production or feigning of physical or psychological signs or symptoms. Unlike malingering, patients are not motivated by secondary gain but rather may seek sympathy, nurturance, and attention

Somatic Symptom and Related Disorders

General Characteristics

- physical signs and symptoms lacking objective medical support in the presence of psychological factors that are judged to be important in the initiation, exacerbation, or maintenance of the disturbance (suffering is out of keeping with what would be normally expected)
- cause significant distress or impairment in functioning
- symptoms are produced unconsciously and are not the result of malingering or factitious disorder, which are disorders of voluntary presentation of symptoms (or intentionally inducing, e.g. injecting feces) for secondary gain
- primary gain: somatic symptom represents a symbolic resolution of an unconscious psychological conflict; serves to reduce anxiety and conflict with no external incentive
- secondary gain: the sick role; external benefits obtained, or unpleasant duties avoided (e.g. work)
- theories for root cause: may represent a masked presentation of a psychiatric issue, amplified perception; social/cultural norms that devalue psychological suffering; lack of ability/language to express distress in a non-somatic way

Management of Somatic Symptom and Related Disorders

- brief, regular scheduled visits with GP to facilitate therapeutic relationship and help patient feel supported (e.g. q4-6 wk)
- good, clear communication among all involved care providers
- limit number of physicians involved in care, minimize medical investigations, coordinate necessary investigations
- emphasis on mechanism of the symptoms and not on the cause while focusing on what the patient can change and control; the psychosocial coping skills, not their physical symptoms (functional recovery > explanation of symptoms)

- focus on functional improvement (physiotherapy, occupational therapy), provide psychoeducation to validate suffering in the face of medically unexplained symptoms
- psychotherapy: CBT, psychodynamic therapy, mindfulness interventions, biofeedback
- minimize psychotropic drugs: anxiolytics for short-term use only (associated with worse outcomes), antidepressants for comorbid depression and anxiety

Somatic Symptom Disorder

DSM-5 DIAGNOSTIC CRITERIA FOR SOMATIC SYMPTOM DISORDER

Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 2013. American Psychiatric Association

A. one or more somatic symptoms that are distressing or result in significant disruption of daily life
B. excessive thoughts, feelings, or behaviours related to the somatic symptoms or associated health concerns as manifested by at least one of the following:
    1. disproportionate and persistent thoughts about the seriousness of one's symptoms
    2. persistently high level of anxiety about health or symptoms
    3. excessive time and energy devoted to these symptoms or health concerns
C. although any one somatic symptom may not be continuously present, the state of being symptomatic is persistent (typically >6 mo)

- **somatic symptom disorder with predominant pain** (previously pain disorder) for those whose somatic symptom is primarily pain
- patients have physical symptoms and believe these symptoms represent the manifestation of a serious illness
- persistent belief despite negative medical investigations and may develop different symptoms over time
- lifetime prevalence may be around 5-7% in the general adult population
- females tend to report more somatic symptoms than males do; cultural factors may influence sex ratio
- other risk factors include: history of sexual abuse, lower education and socioeconomic status, and concurrent psychiatric/chronic physical illnesses
- complications: anxiety and depression commonly comorbid (up to 80%), unnecessary medications, or surgery
- often a misdiagnosis for an insidious illness, so rule out all organic illnesses (e.g. multiple sclerosis)
- DDx: GAD, depressive disorder, delusional disorder, body dysmorphic disorder, obsessive compulsive disorder, other medical condition

Illness Anxiety Disorder

- preoccupation with fear of having, or the idea that one has a serious disease to the point of causing significant impairment
- convictions persist despite negative investigations and medical reassurance; however, able to acknowledge the possibility that feared disease is not present, unlike a delusion, which is fixed and firm
- somatic symptoms are mild or not present (not acute)
- there is a high level of anxiety about health and the individual is easily alarmed about personal health status
- person engages in maladaptive behaviour such as excessive physical checking or total healthcare avoidance
- duration is ≥6 mo; onset in 3rd-4th decade of life
- epidemiology: 3-5% of patients seen by primary care physicians; increased risk of substance use problems
- possible role for SSRIs as treatment due to generally high level of anxiety
- specifiers: care-seeking type or care-avoidant type

Conversion Disorder (Functional Neurological Symptom Disorder)

- one or more symptoms or deficits affecting voluntary motor or sensory function that mimic a neurological or GMC (e.g. impaired coordination, local paralysis, double vision, seizures, or convulsions)
- does not need to be preceded by a psychological event as per previous DSM criteria, however this is still worth exploring as many patients will present after such an event or related to a medical diagnosis in a first-degree relative
- incidence of 2-5 in 100000 in general population; up to 20-25% of neurology inpatients and 5% of psychiatry inpatients
- more common in rural populations and in individuals with little medical knowledge
- spontaneous remission in 95% of acute cases, 50% of chronic cases (>6 mo)
- incompatible findings detected from specific neurological testing can help differentiate between functional and neurological origin (e.g. Hoover's sign and dermatome testing)
- for more details about Conversion Disorder, please consult the DSM-5

Screening questions for somatic disorders

1. When did the symptoms start?
2. Have you been frustrated with getting no answers?
3. What has been your experience with other physicians?
4. What Is your understanding of your symptoms?
5. How have the symptoms affected your life?

Table 7. Differential of Somatic Symptom and Related Disorders

	Somatic Symptom Disorder	Illness Anxiety Disorder	Conversion Disorder	Factitious Disorder	Malingering
Somatic Symptoms	Present	Mild or absent	Neurologic, voluntary motor or sensory	Psychological or physical	Psychological or physical
Symptoms Produced	Unconsciously	Unconsciously	Unconsciously	Consciously	Consciously
Physical Findings	Absent	Absent	Incompatible	Possible, attempts to falsify	Possible, attempts to falsify

La belle indifference: an inappropriately cavalier patient attitude in the face of serious symptoms; classically associated with conversion disorder but is not diagnostic

Hoover's sign: involuntary extension of the "normal" leg occurs when flexing the contralateral leg against resistance

Dissociative Disorders

General Characteristics

- severe dissociation resulting in breakdown of integrated functions of consciousness and perception of self
- severe stress or traumas are predisposing factors for dissociative disorders (e.g. victims of significant or chronic trauma, child abuse)
- result in significant distress or impairment in social/occupational functioning
- psychotherapy (psychodynamic, CBT) are the mainstays of treatment; lack of evidence for use of medications
- DDx: PTSD, acute stress disorder, borderline personality disorder, somatic symptom disorder, substance use disorder, GMC (various neurologic disorders including complex/partial seizures, migraine, Cotard syndrome)

Dissociative Identity Disorder

- disruption of identity characterized by ≥2 distinct personality states or an experience of possession
- can manifest as sudden alterations in sense of self and agency (ego-dystonic emotions, behaviours, speech)
- features recurrent episodes of amnesia (declarative or procedural) as well as episodes of depersonalization and derealization
- rare (<1%); can manifest at any age, although childhood physical/sexual abuse or neglect is a major risk factor
- caution: high-risk of attempting suicide and/or self-harm
- DDx includes borderline personality disorder and PTSD

Dissociative Amnesia

- inability to recall important autobiographical information, usually of a traumatic or stressful nature that is inconsistent with normal forgetting and not attributable to a psychiatric disorder, medical illness, or effects of a substance
- localized/selective amnesia: failure to recall all/some events during a prescribed period of time (however procedural memory is preserved)
- can experience periods of flashbacks or nightmares related to associated trauma, increased risk of suicide as amnesia resolves
- generalized amnesia (more rare): complete loss of memory for one's life history, ± procedural knowledge, ± semantic knowledge; usually sudden onset; often presents with perplexity, disorientation, and aimless wandering

Dissociative Fugue
Sudden unexpected travel away from home that is accompanied by amnesia for identity or other autobiographical details

Depersonalization/Derealization Disorder

- persistent or recurrent episodes of one or both of:
  - depersonalization: experiences of detachment from oneself, feelings of unreality, or being an outside observer to one's thoughts, feelings, speech, and actions (can feature distortions in perception including time, as well as emotional and physical numbing)
  - derealization: experiences of unreality or detachment with respect to the surroundings (i.e. feeling as if in a dream, or that the world is not real; external visual world is foggy or distorted)
- transient (s-h) experiences of this nature are quite common in the general population
- episodes can range from h-yr, patients are often quite distressed and verbalize concerns of "going crazy"

During depersonalization (detachment from one's self) or derealization (detachment from one's surroundings), patients usually have intact reality testing, which adds to their alarming nature

Sleep Disorders

- for more information regarding normal sleep cycles and the illnesses described, see Neurology, *Sleep Disorders*, N48

Overview

- adequate sleep is essential to normal functioning; deprivation can lead to cognitive impairment and increased mortality
- circadian rhythms help regulate mood and cognitive performance
- neurotransmitters commonly implicated in psychiatric illnesses also regulate sleep
  - increased ACh activity and decreased activity of monoamine neurotransmitters is associated with greater REM sleep
  - decreased adrenergic and cholinergic activity are associated with NREM sleep
- depression is associated with decreased Δ (deep, slow-wave) sleep, decreased REM latency, and increased REM density
- criteria for sleep disorders:
  - must cause significant distress or impairment in normal functioning
  - not due to a General Medical Condition (GMC) or medications/drugs (unless specified)

Management

- sleep hygiene is a simple, effective, but often underutilized method for addressing sleep disturbances; recommendations include:
  - waking up and going to bed at same time every day, including on weekends
  - avoiding long periods of wakefulness in bed
  - not using bed for non-sleep activities (reading, TV, work)
  - avoiding screens, especially smartphones and iPads in the hour before bed
  - avoiding napping
  - discontinuing or reducing consumption of alcohol, caffeine, drugs
  - exercising at least 3-4x/wk (but not in the evening, if this interferes with sleep)
- cognitive behavioural therapy for insomnia (CBTi) is considered first-line treatment for chronic insomnia
- pharmacological treatments are illness-specific
  - avoid benzodiazepenes: increased risk of abuse/dependence, rebound anxiety/insomnia, cognitive impairment, daytime somnolence, and disturbed sleep architecture (suppresses deep and REM sleep)
  - non-benzodiazepines (e.g. zopiclone/eszopiclone/zolpidem, lemborexant, low dose doxepin) are preferred and effective for short-term treatment; they should be re-evaluated regularly as long-term use is associated with dependency
  - "z-drugs": common side-effect is bitter metallic taste, which is improved by something acidic such as orange juice; high doses increase risk of cognitive impairment and falls (particularly among the elderly)
  - lemborexant (orexin receptor antagonist) reduces wake pressure/drive, as opposed to increasing sleep pressure/drive with other sedating agents; avoid use in patients with narcolepsy or cataplexy
  - trazodone, mirtazapine, and quetiapine can be prescribed off-label if there are comorbid psychiatric symptoms
  - low-dose amitriptyline can be prescribed for patients with comorbid pain
  - screen for complex sleep behaviours before and after prescribing a medication for insomnia
  - consider whether sleep issue is part of another psychiatric or medical illness and treat those conditions

Table 8. Major DSM-5 Sleep-Wake Disorders

Note: For more information regarding specific disorders, see Neurology, *Sleep Disorders*, N48; Family Medicine, *Sleep Disorders*, FM48; and Respirology, *Sleep Apnea*, R29

Category	Disorder	Description	Management
Dyssomnias (insufficient, excessive, or altered timing of sleep)	**Insomnia disorder**	Difficulty initiating/maintaining sleep or early-morning awakening with inability to return to sleep; can be acute or chronic (≥3 mo)	Sleep hygiene measures CBT for insomnia Non-benzodiazepines are first-line ("z-drugs", lemborexant, low dose doxepin)
	Hypersomnolence disorder	Excessive daytime sleepiness despite sleeping at least 7 h; difficulty being fully awake after awakening at least 3 times per wk for at least 3 mo	Modafinil or stimulant drugs Scheduled napping
	Narcolepsy	Classic tetrad consists of recurrent attacks of irrepressible need to sleep (sleep attacks), REM-related sleep phenomena, hypnagogic or hypnopompic hallucinations, and cataplexy (sudden loss of tone evoked by strong emotion without LOC)	Sleep hygiene Amphetamines (methamphetamine) Non-amphetamines (Modafinil, sodium oxybate)
	Circadian rhythm sleep-wake disorders	Insomnia or excessive sleepiness due to misalignment or alteration in endogenous circadian rhythm	Melatonin Bright light phototherapy Modafinil if severe
	Restless legs syndrome	Uncomfortable, frequent urge to move legs at night; relief with movement and aggravation with inactivity	Dopamine agonists and benzodiazepines are first-line Replace iron if low ferritin Modify medications that may be exacerbating symptoms
	Substance/medication-induced sleep disorder	Disturbance in sleep (insomnia or daytime sleepiness) caused by substance/medication intoxication or withdrawal	
Breathing-Related Sleep Disorders	**Obstructive sleep apnea hypopnea**	Breathing issues due to repetitive collapse of the upper airway during sleep - resulting in nonrestorative sleep and excessive daytime sleepiness; snoring, disrupted sleep, and morning headaches are common signs	Continuous positive airway pressure (CPAP) Weight loss/exercise Surgery
	Central sleep apnea	Breathing issues due to aberrant brain signaling More common among chronic opioid users	CPAP/bilevel positive airway pressure (BiPAP) Supplemental oxygen
	Sleep-related hypoventilation	Breathing issues due to decreased responsiveness to carbon dioxide levels (decreased respiration)	CPAP/BiPAP Medications that support breathing
Parasomnias (unusual sleep-related behaviours)	**Non-rapid eye movement sleep arousal disorders**	Incomplete awakening from sleep, complex motor behaviour without conscious awareness; amnesia regarding episodes; includes symptoms of:	
		Sleepwalking: rising from bed and walking about, blank face, unresponsive, awakened with difficulty	Most cases do not require treatment aside from addressing precipitating factors and education regarding sleep hygiene Severe cases may respond to low-dose clonazepam
		Sleep terrors: recurrent episodes of abrupt terror arousals from sleep, usually beginning with a panicky scream, intense fear, and autonomic arousal; relative unresponsiveness to comfort during episodes	Often self-limited and benign
		Specifiers: sleep-related sexual behaviour (sexsomnia) and sleep-related eating	
	Nightmare disorder	Repeated extended, extremely dysphoric, often very vivid, well-remembered dreams that usually involve significant threats; rapid orientation and alertness on awakening with autonomic arousal	Reassurance Desensitization/imagery rehearsal therapy Prazosin can be helpful for those with PTSD
	Rapid eye movement sleep behaviour disorder	Arousal during sleep, associated with vocalization and/or complex motor behaviours; can cause violent injuries; rapid orientation and alertness on awakening	Melatonin Clonazepam Discontinuation of causative medications such as TCAs, SSRIs and SNRIs

Sexuality and Gender

Gender Dysphoria

Definition

- discomfort or distress caused by a discrepancy between sex assigned at birth and a person's gender identity
- gender identity refers to a person's intrinsic sense of self as male, female, both, neither, or anywhere along the spectrum
- for more details about Gender Dysphoria, please consult the DSM-5

Clinical Features

- strong and persistent cross-gender identification
- desire to be rid of primary/secondary sex characteristics and to gain the primary/secondary sex characteristics of their identified gender
- repeated stated desire or insistence that one is of the opposite sex

- preference for cross-dressing, cross-gender roles in make-believe play
- intense desire to participate in the stereotypical games and pastimes of the opposite sex
- strong preference for playmates of the opposite sex
- significant distress or impairment in functioning and persistent discomfort with his or her sex or gender role

Management
- supportive psychotherapy or other mental health counselling
- hormone therapy with feminizing (e.g. estrogen and anti-androgen) or masculinizing (e.g. testosterone) agents
- gender affirming surgery

Paraphilic Disorders

Definition
- intense and persistent sexual arousal, over a period of at least 6 mo, that is elicited by something other than genital stimulation or preparatory fondling with phenotypically normal, physically mature, consenting human partners
- paraphilic disorder: when paraphilia causes distress or functional impairment to the individual, or a paraphilia whose realization entails personal harm or risk of harming others

Clinical Features
- begins in childhood or early adolescence; increasing complexity and stability with age
- tends to be chronic but decreases in intensity with advancing age; may increase with stress
- rarely self-referred; come to medical attention through interpersonal or legal conflict
- person usually has more than one paraphilia; more common in men (only 5% of patients with paraphilia are women)
- subtypes:
  - voyeuristic - sexual arousal when spying intentionally on unsuspecting individuals
  - exhibitionistic - sexual arousal from the act or fantasy of exposing one's genitals to non-consenting individuals
  - frotteuristic - sexual arousal from touching or rubbing one's genitals up against non-consenting individuals
  - sexual masochism - sexual arousal from being humiliated, beaten, bound, or otherwise made to suffer
  - sexual sadism - sexual arousal from the psychological or physical suffering of a victim including humiliation
  - pedophilic - sexual attraction to prepubescent children - may be exclusive (only children) or nonexclusive (children and adults)
  - fetishistic - recurrent, intense sexual arousal from an inanimate object or specific focus on a non-genital body part(s)
  - transvestic - sexual arousal from act or fantasies of cross-dressing
  - other specified paraphilic disorder or unspecified paraphilic disorder

Management
- anti-androgen drugs (e.g. medroxyprogesterone or leuprolide)
- SSRIs (e.g. high-dose fluoxetine)
- behaviour modification
- psychotherapy

Sexual Addiction

- definition: engaging in persistent and escalating patterns of sexual behaviour, despite increasing negative consequences to self and others
- clinical features: may be characterized by compulsive searching for multiple sexual partners, persistent thoughts of or craving for sex to the detriment of other activities, compulsive masturbation, extensive use of pornography, compulsive sexuality in a relationship, and feelings of remorse or guilt after sex
- management: CBT, 12-step programs, SSRIs to reduce libido

Sexual Dysfunction

- important to identify treatable causes (e.g. atrophic vaginitis, diabetes, antidepressant medications)
- see Gynaecology, GY34 and Urology, U33

Eating Disorders

Definition
- eating disorders are characterized by a persistent disturbance of eating that impairs psychosocial functioning or health
- disorders include: anorexia nervosa, avoidant/restrictive food intake disorder, binge eating disorder, bulimia nervosa, pica, and rumination disorder

Epidemiology
- anorexia nervosa (AN): 1% of adolescent and young adult females; 0.3% males; onset in mid-teens (14-18 yr)
- bulimia nervosa (BN): 2-4% of adolescent and young adult females; 0.5% males; onset in late teens or early adulthood
- F:M=10:1; mortality of AN 5-10%
- common comorbidities: depression (50-75%), substance misuse (35% in BN, 15% in AN), OCD (25% in AN)

Etiology
- multifactorial: psychological, sociological, and biological associations
- individual: perfectionism, lack of control in other life areas, history of sexual abuse
- personality: anxiety, perfectionism, obsessionality, negative emotionality, cognitive inflexibility
- family & sociocultural: invalidating family structure, prevalent in industrialized societies, idealization of thinness in the media, athletic demands
- puberty
- genetic factors
  - AN: 6% prevalence in siblings, with one study of twin pairs finding concordance in 9 of 12 monozygotic pairs vs. concordance in 1 of 14 dizygotic pairs (10x greater risk among first-degree relatives)
  - BN: higher familial incidence of affective disorders than the general population

Risk Factors
- physical factors: obesity, chronic medical illness (e.g. DM)
- psychological factors: individuals who by career choice are expected to be thin, family history (mood disorders, eating disorders, substance use disorder), history of sexual abuse (especially for BN), competitive athletes, concurrent associated mental illness (depression, OCD, anxiety disorder (especially panic and agoraphobia), substance use disorder (specifically for BN))

Complications
- growth delay, osteoporosis (40%), osteopenia (50%), cardiovascular complications (bradycardia, QTc prolongation, starvation edema), gastrointestinal complications (irritable bowel syndrome, constipation, gastric dilation), electrolyte disturbances (hypokalemia, hypomagnesemia, hypophosphatemia), refeeding syndrome, and endocrine abnormalities (increased GH, reduced LH, FSH, and T3)

Eating Disorder Screening
Method to identify patients with eating disorders. A "Yes" to two or more questions is associated with a sensitivity and specificity of 78 and 88%, respectively

SCOFF
- Do you make yourself **S**ick because you feel uncomfortably full?
- Do you worry you have lost **C**ontrol over how much you eat?
- Have you recently lost more than **O**ne stone (14 pounds or 6.35 kg) in a 3 mo period?
- Do you believe yourself to be **F**at when others say you are too thin?
- Would you say that **F**ood dominates your life?

Anorexia Nervosa

DSM-5 DIAGNOSTIC CRITERIA FOR ANOREXIA NERVOSA
Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, 5th ed. 2013. American Psychiatric Association

A. restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. Significantly low weight is defined as a weight that is less than minimally normal or, for children and adolescents, less than that minimally expected
B. intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain, even though at a significantly low weight
C. disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight

- **specifiers**: partial remission, full remission, severity based on BMI (mild = BMI >17 kg/m^2, moderate = BMI 16-16.99 kg/m^2, severe = BMI 15-15.99 kg/m^2, extreme = BMI <15 kg/m^2), type (restricting = during last 3 mo no episodes of binge-eating or purging vs. binge-eating/purging type = in last 3 mo have participated in recurrent episodes of binge-eating/purging)

Athletic Triad
Disordered eating
Amenorrhea
Osteoporosis

Some patients with insulin-dependent DM may stop their insulin in order to lose weight

Management
- standard work-up: vitals (weight and orthostatic BP and HR), bloodwork (CBC, electrolytes, creatinine, liver enzymes, B_{12}, TSH), ECG
- psychotherapy: individual, group, family; address food and body perception, coping mechanisms, health effects
- CBT: sets clear weight goals and expectations, makes use of recording sheets, targets maintaining factors such as negative body image
- family-based treatment is primarily used in the paediatric system, main focus is on weight restoration and return to physical health
- medications of little value; however, SSRIs may be helpful in treating concurrent mood and anxiety disorders
- outpatient and inpatient programs are available (nutritional rehabilitation)
- inpatient psychiatric hospitalization for treatment of eating disorders is rarely on an acute basis (unless there is a concurrent psychiatric reason for emergent admission (e.g suicide risk)). Such patients often require a specialized ED program.
- criteria to admit to medical ward for hospitalization: <65% of standard body weight (<85% of standard body weight for adolescents), hypovolemia requiring intravenous fluid, heart rate <40 bpm, abnormal serum chemistry (e.g. low K^+, low Mg^{2+}, Low PO_4^{3-}, high creatinine), or if actively suicidal
- agree on target body weight on admission and reassure this weight will not be surpassed
- monitor for complications of AN (see Table 9, PS42)
- monitor for refeeding syndrome
  - potentially life-threatening metabolic response to refeeding in severely malnourished patients resulting in severe shifts in fluid and electrolyte levels
  - complications include hypophosphatemia, congestive heart failure, cardiac arrhythmias, delirium, and death
  - prevention: slow refeeding, gradual increase in nutrition, supplemental phosphorus, and close monitoring of electrolytes and cardiac status

Prognosis
- adolescent onset has much better prognosis than adult onset
- only about 50% make a full recovery
- with treatment, 70% resume a weight of at least 85% of expected levels and about 50% resume normal menstrual function
- eating peculiarities and associated psychiatric symptoms are common and persistent
- high rates of mortality (7%) secondary to severe and chronic starvation, metabolic or cardiac catastrophes, with a significant proportion dying by suicide

Bulimia Nervosa

DSM-5 DIAGNOSTIC CRITERIA FOR BULIMIA NERVOSA
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A. recurrent episodes of binge-eating; an episode of binge-eating is characterized by both of the following:
   - eating, in a discrete period of time, an amount of food that is definitely larger than what most individuals would eat during a similar period of time and under similar circumstances
   - a sense of lack of control over eating during the episode

B. recurrent inappropriate compensatory behaviour in order to prevent weight gain, such as self-induced vomiting, misuse of laxatives, diuretics, enemas, or other medications, fasting, or excessive exercise

C. the binge-eating and inappropriate compensatory behaviours both occur, on average, at least once a week for 3 mo

D. self-evaluation is unduly influenced by body shape and weight

E. the disturbance does not occur exclusively during episodes of AN

- **specifiers**: partial remission, full remission, severity (mild = 1-3 inappropriate compensatory behaviours/wk, moderate = 4-7 inappropriate compensatory behaviours/wk, severe = 8-13 inappropriate compensatory behaviours/wk, extreme = 14+ inappropriate compensatory behaviours/wk)

Associated Features
- fatigue and muscle weakness due to repetitive vomiting and fluid/electrolyte imbalance
- tooth decay, perioral irritation, mouth ulcers
- swollen appearance around angle of jaw and puffiness of eye sockets due to fluid retention, edema
- reddened knuckles, Russell's sign (knuckle callus from self-induced vomiting)
- trouble concentrating, fatigue, headache, abdominal pain/reflux
- weight fluctuation over time

Management
- medical admission for significant electrolyte abnormalities
- biological: treatment of starvation effects, SSRIs (60 mg fluoxetine has the most evidence) as adjunct
- psychological: develop trusting relationship with therapist to explore personal etiology and triggers, CBT, family therapy, recognition of health risks
- social: challenge destructive societal views of women, use of hospital environment to provide external patterning for normative eating behaviour

Prognosis
- relapsing/remitting disease
- good prognostic factors: onset before age 15, achieving a healthy weight within 2 yr of treatment
- poor prognostic factors: later age of onset, previous hospitalizations, individual and familial disturbance
- 60% good treatment outcome, 30% intermediate outcome, 10% poor outcome (mortality rate of approximately 2% per decade)

Binge-Eating Disorder

Definition
- recurrent episodes of binge-eating (as defined by criteria A of BN) that are associated with eating much more rapidly than normal, eating until feeling uncomfortably full, eating large amounts when not physically hungry, eating alone because embarrassed by how much one is eating, and/or feeling disgusted with oneself/depressed/very guilty afterwards at least once/wk x 3 mo
- not associated with any compensatory behaviours
- dieting usually follows binge-eating (vs. BN where dysfunctional dieting typically precedes binge-eating)
- for more details about Binge-Eating Disorder, please consult the DSM-5

Epidemiology
- F:M=2:1
- begins in adolescence or young adulthood

Treatment
- CBT

Avoidant/Restrictive Food Intake Disorder

Definition
- eating/feeding disturbance (i.e. apparent lack of interest in eating or food) to the extent of persistent failure to meet appropriate nutritional and/or energy needs, resulting in significant weight loss/growth failure and nutritional deficiencies; patients experience disturbances in psychosocial functioning and may become dependent on enteral feeding/oral nutritional supplementation
  - does not occur during an episode of AN or BN and not better explained by lack of available food or culturally sanctioned practice
  - no evidence of distress in the way in which one's body weight or shape is experienced

Risk Factors
- temperament (e.g. anxiety disorders), environment (e.g. familial anxiety), genetic (e.g. history of GI conditions)
- begins in infancy and can persist into adulthood

Treatment
- psychoeducation
- behaviour modification
- psychotherapy

Points for Differentiating Between Eating Disorders
- AN of binge-eating/purging type (significantly low body weight) takes priority over a BN diagnosis (body weight not in criteria)
- BN requires compensatory behaviours
- Binge-eating disorder does not involve compensatory behaviours
- Avoidant/restrictive food intake disorder does not involve disturbances in body image

Table 9. Physiologic Complications of Eating Disorders

System	Starvation/Restriction	Binge-Purge
General	Low BP	Russell's sign (knuckle callus)
	Low HR	Parotid gland enlargement
	Significant orthostatic changes ± syncopal episodes Low body temperature	Perioral skin irritation and mouth ulcers
	Vitamin deficiencies	Periocular and palatal petechiae
	Emaciation	Loss of dental enamel and caries
	Sleep disturbances	Aspiration pneumonia
	Fatigue/weakness	Metabolic alkalosis secondary to hypokalemia and loss of acid
		Fatigue
Endocrine	Primary or secondary amenorrhea, cold intolerance, decreased T3/T4	
Neurologic	Seizure (decreased Ca^{2+}, Mg^{2+}, PO_4^{3-})	
Cutaneous	Dry skin, lanugo hair, hair loss or thinning, brittle nails, yellow skin from high carotene	
GI	Constipation, GERD, delayed gastric emptying, abdominal pain	Acute gastric dilation/rupture, pancreatitis, GERD, hematemesis secondary to Mallory-Weiss tear
CVS	Arrhythmias, CHF	Arrhythmias, cardiomyopathy (from use of ipecac), sudden cardiac death (decreased K^+)
MSK	Osteoporosis secondary to hypogonadism	Muscle wasting
Renal	Pre-renal failure (hypovolemia), renal calculi	Renal failure (electrolyte disturbances)
Extremities	Pedal/periorbital edema (decreased albumin)	Pedal/periorbital edema (decreased albumin)
Lab Values	Starvation: decreased RBCs, decreased WBCs, decreased LH, decreased FSH, decreased estrogen, decreased testosterone, increased GH, increased cholesterol	Vomiting: decreased Na^+, decreased K^+, decreased Cl^-, decreased H^+, increased amylase; hypokalemia with metabolic alkalosis
	Dehydration: increased BUN	Laxatives: decreased Na^+, decreased K^+, decreased Cl^-, increased H^+; metabolic acidosis

Important electrolytes in eating disorders: KPMg (potassium, phosphate, magnesium)

Personality Disorders

- in the literature, personality and its disorders can be understood using a trait-based dimensional approach (i.e. 5 major traits such as extraversion, agreeableness, conscientiousness, neuroticism, and openness to experiences rated on a continuum of dysfunctional effects) rather than discrete categories; however, the discrete categories still remain in the current DSM and will be referenced here

A flag for personality disorders in clinical setting is the reaction that a patient is eliciting in you

General Information

- an enduring pattern of inner experience and behaviour that deviates markedly from the expectations of the individual's culture; manifested in two or more of: cognition, affect, interpersonal functioning, impulse control
- inflexible and pervasive across a range of situations
- pattern is stable and well-established by adolescence or early adulthood (i.e. not a sudden onset)
- associated with many comorbidities such as depression, suicide, violence, brief psychotic episodes, substance use, and treatment resistance
- relationship building and establishing boundaries are important; focus should be placed on validating, finding things to be truly empathetic about, and speaking to the patient's strengths
- mainstay of treatment is psychotherapy (e.g. CBT, interpersonal psychotherapy, psychodynamic psychotherapy, DBT); add pharmacotherapy to treat associated psychiatric disorders (e.g. depression, anxiety, substance misuse)

Personality disorders with familial associations: schizotypal, antisocial, and borderline

Classification

- personality disorders are divided into three clusters (A, B, and C), with shared features among disorders within each

Table 10. Description and Diagnosis of Personality Disorders

Cluster A: "Mad" Personality Disorders
- Patients seem odd, eccentric, withdrawn
- Familial association with psychotic disorders
- Common defense mechanisms: intellectualization, projection, magical thinking

Paranoid Personality Disorder (1-4% of general population)
Pervasive distrust and suspiciousness of others, interpret motives as malevolent
Blame problems on others and seem angry and hostile
Diagnosis requires 4+ of: **SUSPECT**
1. **S**uspicious that others are exploiting or deceiving them (without sufficient basis)
2. **U**nforgiving (bears grudges)
3. **S**pousal infidelity suspected without justification
4. **P**erceive attacks on character, counterattacks quickly
5. **E**nemies or friends? Preoccupied with acquaintance trustworthiness
6. **C**onfiding in others is feared
7. **T**hreats interpreted in benign remarks
(Note: Must rule out psychotic disorder where no true delusions or hallucinations present)

Schizotypal Personality Disorder (4-5% of general population)
Pervasive pattern of social and interpersonal deficits, cognitive/perceptual distortions, eccentric behaviours, and peculiar thought patterns
Diagnosis requires 5+ of: **ME PECULIAR**
1. **M**agical thinking
2. **E**xperiences unusual perceptions (including body illusions)
3. **P**aranoid ideation
4. **E**ccentric behaviour or appearance
5. **C**onstricted or inappropriate affect
6. **U**nusual thinking/speech (e.g. vague, stereotyped)
7. **L**acks close friends
8. **I**deas of reference
9. **A**nxiety in social situations that does not diminish with familiarity (related to fears)
(Note: **R**ule out psychotic/pervasive developmental disorders - this is not part of the criteria; the more fixed and systematic a belief is, the more likely it is of delusional intensity)

Schizoid Personality Disorder (3-5% of general population)
Neither desires nor enjoys close relationships including being a part of a family; prefers to be alone. Lifelong pattern of social withdrawal. Seen as eccentric and reclusive with restricted affect in a variety of contexts
Diagnosis requires 4+ of: **DISTANT**
1. **D**etached/flat affect, emotionally cold
2. **I**ndifferent to praise or criticism
3. **S**exual experiences of little interest
4. **T**asks done solitarily
5. **A**bsence of close friends (other than first-degree relatives)
6. **N**either desires nor enjoys close relationships (including family)
7. **T**akes pleasure in few (if any) activities

Cluster B: "Bad" Personality Disorders
- Patients seem dramatic, emotional, inconsistent, and impulsive
- Sensitive to perceived criticism, abandonment, or lack of attention; difficulty with interpersonal relationships due to self-serving, hostile, or erratic behaviour
- Familial association with mood disorders
- Common defense mechanisms: denial, acting out, regression (histrionic PD), splitting (borderline PD), projective identification, idealization/devaluation

Borderline Personality Disorder (1-2% of general population)
A pervasive pattern of instability of interpersonal relationships, self-image, and affects; marked impulsivity
Strong correlation with a history of childhood sexual abuse. Characterized by interpersonal, cognitive, behavioural, and affective deficits. Often exposed to an emotionally invalidating environment. The more dramatic behaviour tends to diminish as patients age. DBT is the principal treatment (see *Psychotherapy*, PS50)
10% suicide rate
Diagnosis requires 5+ of: **IMPULSIVE**
1. **I**mpulsive (minimum of 2 self-damaging ways, e.g. sex/drugs/spending)
2. **M**ood/affect instability
3. **P**aranoia or dissociation under stress
4. **U**nstable self-image
5. **L**abile intense relationships (extremes of idealization and devaluation)
6. **S**uicidal gestures/self-harm
7. **I**nappropriate anger
8. **V**oiding abandonment (real or imagined, frantic efforts to)
9. **E**mptiness (feelings of)
(Note: More frequently diagnosed in females but research suggests equal gender distribution)

Narcissistic Personality Disorder (around 6% of general population)
Sense of superiority, needs constant admiration, lacks empathy, but with fragile sense of self. Consider themselves "special" and will exploit others for personal gain. Beginning by early adulthood and present in a variety of contexts
Diagnosis requires 5+ of: **GRANDIOSE**
1. **G**randiose sense of self-importance (e.g. exaggerates achievements and talents)
2. **R**equires excessive admiration
3. **A**rrogant
4. **N**eeds to be special (and associate with other special or high-status people)
5. **D**reams of success, power, beauty, love (preoccupied with these fantasies)
6. **I**nterpersonally exploitative
7. **O**thers (lacks empathy, unable to recognize feelings/needs of others)
8. **S**ense of entitlement
9. **E**nvious (or believes others are envious)

Antisocial Personality Disorder (M: 2-4%, F: 0.5-1%)
Lack of remorse for actions, manipulative and deceitful, often violate the law. May appear charming on first impression. Pervasive pattern of disregard for others and violation of others' rights must be present before age 15; however, for the diagnosis of ASPD patients must be at least 18. Must have evidence of conduct disorder before age 15, history of trauma/abuse common (see *Child Psychiatry*, PS44)
Diagnosis requires 3+ of: **CORRUPT**
1. **C**annot conform to law and/or social norms (repeated illegal acts)
2. **O**bligations ignored (irresponsible)
3. **R**eckless disregard for safety of self or others
4. **R**emorseless
5. **U**nderhanded (deceitful; conning others for personal profit or pleasure)
6. **P**lanning insufficient (impulsive)
7. **T**emper (irritable and aggressive)

Histrionic Personality Disorder (2% of general population)
Attention-seeking behaviour and excessively emotional. Are dramatic, flamboyant, and extroverted. Cannot form meaningful relationships. Often sexually inappropriate. Diagnosed more in females but studies suggest equal prevalence
Diagnosis requires 5+ of: **ACTRESSS**
1. **A**ppearance used to attract attention
2. **C**entre of attention (else uncomfortable)
3. **T**heatrical
4. **R**elationships (believed to be more intimate than they are)
5. **E**asily influenced
6. **S**eductive behaviour
7. **S**hallow expression of emotions (which rapidly shift)
8. **S**peech (impressionistic and vague)

Table 10. Description and Diagnosis of Personality Disorders

Cluster C: "Sad" Personality Disorders
- Patients seem anxious, fearful
- Familial association with anxiety disorder
- Common defense mechanisms: isolation, avoidance, hypochondriasis

Avoidant Personality Disorder (2.4% of general population)
Timid and socially awkward with a pervasive sense of inadequacy, social inhibition, and hypersensitivity to criticism. Fear of embarrassing or humiliating themselves in social situations so remain withdrawn and socially inhibited
Diagnosis requires 4+ of: **CRINGES**
1. **C**riticism or rejection preoccupies thoughts in social situations
2. **R**estraint in relationships due to fear of being shamed
3. **I**nhibited in new relationships due to fear of inadequacy
4. **N**eeds to be sure of being liked before engaging socially
5. **G**ets around occupational activities requiring interpersonal contact
6. **E**mbarrassment prevents new activity or taking risks
7. **S**elf-viewed as unappealing or inferior

Obsessive-Compulsive Personality Disorder (2.1-7.9%)
Preoccupation with orderliness, perfectionism, and mental and interpersonal control. Is inflexible, closed-off, and inefficient
Highly comorbid with mood/anxiety and eating disorders
Diagnosis requires 4+ of: **SCRIMPER**
1. **S**tubborn
2. **C**annot discard worthless objects
3. **R**ule/detail obsessed (to point of activity lost)
4. **I**nflexible in matters of morality, ethics, values
5. **M**iserly
6. **P**erfectionistic to the extent that it hampers task completion
7. **E**xcludes leisure due to devotion to work
8. **R**eluctant to delegate to others

Dependent Personality Disorder (0.5-0.6% of general population)
Pervasive and excessive need to be taken care of, excessive fear of separation, clinging and submissive behaviours. Difficulty making everyday decisions. Useful to set regulated treatment schedule (regular, brief visits) and being firm about in between issues. Encourage patient to do more for themselves, engage in own problem-solving
Diagnosis requires 5+ of: **RELIANCE**
1. **R**eassurance and/or advice required for everyday decisions (excessive)
2. **E**xpressing disagreement difficult
3. **L**ife responsibilities assumed by others
4. **I**nitiating projects difficult (because lack of self-confidence)
5. **A**lone (feels helpless and uncomfortable when alone)
6. **N**urturance (goes to excessive lengths to obtain)
7. **C**ompanionship sought urgently
8. **E**xaggerated fears of being left to care for self

Table 11. Key Differences Among Schizoid, Schizotypal, and Schizophrenia

	Schizoid	Schizotypal	Schizophrenia
Thought Form	Organized	Organized, but vague and circumstantial	Disorganized, tangential, loosening of associations
Thought Content	No psychosis	No psychosis; may have ideas of reference, paranoid ideation, odd beliefs, and magical thinking	Psychosis
Relationships	Solitary, NO desire for social relationships	Lacks close relationships, INTERESTED in relationships but has difficulty forming them	Socially marginalized, but not by choice

OCPD vs. OCD

	OCPD	OCD
Ego-Syntonic or Ego-Dystonic	Ego-syntonic	Ego-dystonic
Thought Content	Obsessional thinking, no compulsions, strict routine and rigidity in day-to-day matters, more perfectionistic and rigid	Obsessions and compulsions, rituals, anxiety provoking unwanted intrusive thoughts

Child Psychiatry

Developmental Concepts

- temperament: a child's innate psycho-physiological and behavioural characteristics (i.e. emotionality, activity, and sociability); spectrum from "difficult" to "slow-to-warm-up" to "easy temperament"
- parental fit: the congruence between parenting style (authoritative, permissive) and child's temperament
- attachment: special relationship between child and primary caretaker(s); develops during first year, the caretaker's attachment style is the best predictor of their child's attachment style, see Table 12
- separation anxiety (normal between 10-18 mo): where separation from attachment figure results in distress

Table 12. Attachment Models

Parent/Caregiver	Attachment Type	Features in Child (during Strange Situation experiment)
Loving, consistently available, sensitive, and receptive	Secure	Freely explores and engages with strangers well (as long as mother in close proximity), upset with caregiver's departure, happy with return
Rejecting, unavailable psychologically, insensitive responses	Insecure (avoidant)	Ignores caregiver, shows little emotion with arrival or departure, little exploration
Inconsistent, insensitive responses, role reversal	Insecure (ambivalent/resistant)	Clingy but inconsolable, often displays anger or helplessness, little exploration
Frightening, dissociated, sexualized, or atypical **Often history of trauma or loss**	Disorganized	Simultaneous approach/avoidance and stress-related straining behaviour

Consider speaking to children alone. Always consider child abuse in your DDx.
See Paediatrics, P18

Tips for the Child Interview
- Use language the child will understand (e.g. don't ask about feelings of worthlessness, ask about whether they feel like they are a bad kid)
- Use developmentally-appropriate questions (e.g. don't ask about lack of interest in activities, ask children whether they feel bored)

Mood Disorders in Children and Adolescents

MAJOR DEPRESSIVE DISORDER

HEEADSSS Interview
Home environment
Education/Employment
Eating
Activities
Drugs
Sex
Safety
Suicide/depression

Epidemiology
- lifetime prevalence for pre-pubertal 1-2% (F:M=1:1); adolescents 4-18% (F:M=2:1)

Clinical Features
- only difference in diagnostic criteria for children and adolescents is that irritable mood may replace depressed mood
- physical features: insomnia (children), hypersomnia (adolescents), somatic complaints, substance misuse, decreased hygiene
- psychological features: irritability, boredom, anhedonia, low self-esteem, deterioration in academic performance, social withdrawal, lack of motivation, listlessness
- common comorbid diagnoses: anxiety, ADHD, ODD, conduct disorder, eating disorders, and substance misuse

Treatment
- majority never seek treatment
- supportive therapy including psychoeducation, active listening, and lifestyle advice helpful in mild depressive episode
- CBT or IPT, internet-based therapy if in-person options unavailable
- 1st line SSRI: fluoxetine
- 2nd line SSRIs: escitalopram, sertraline, citalopram
- close follow-up for adolescents starting SSRIs to monitor for increased suicidal ideation or behaviour
- in severe depression, best evidence for combined pharmacotherapy and psychotherapy
- ECT or rTMS: limited evidence in this population, only for use in adolescents ≥12 y/o with severe illness, psychotic features, catatonic features, persistently suicidal
- light therapy, self-help books, and applications can be used as adjuncts

Prognosis
- prolonged episodes, up to 1-2 yr = poor prognosis
- prognosis variable; adolescents with depression more likely to have depression in adulthood than adolescents without
- approximately 2% of adolescents with depression will develop bipolar disorder within 4 yr
- complications: negative impact on family and peer relationships, school failure, significantly increased risk of suicide attempt or completion (however, suicide risk low for pre-pubertal children), substance use disorder

DISRUPTIVE MOOD DYSREGULATION DISORDER

Clinical Features
- severe, developmentally inappropriate, recurrent verbal or behavioural temper outbursts at least 3x/wk with persistently irritable mood in between
- symptom onset before age 10, occurring for ≥12 mo, in ≥2 settings, with no more than 3 consecutive mo free from symptoms
- diagnosis should be made between ages 6-18
- criteria not met for intermittent explosive disorder nor bipolar disorder (no mania/hypomania)
- supersedes diagnosis of ODD if criteria for both are met
- common comorbidities: ADHD, anxiety disorders, depressive disorders

BIPOLAR DISORDER

Clinical Features
- mixed presentation and psychotic symptoms (hallucinations and delusions) more common in adolescent population than adult population
  - often misdiagnosed in the adolescent population
- unipolar depression may be an early sign of adult bipolar disorder
- associated with rapid onset of depression, psychomotor retardation, mood-congruent psychosis, affective illness in family, and pharmacologically-induced mania

Treatment
- lack of research in adolescent population, treatment guidelines based off of adult recommendations
- pharmacotherapy: mood stabilizers (lithium, anticonvulsants) and/or antipsychotics (risperidone, olanzapine, quetiapine, aripiprazole)
- psychotherapy: CBT, family-focused therapy (a therapeutic modality designed for bipolar disorder that combines psychoeducation, communication skills training, and problem-solving skills training)

Anxiety Disorders in Children and Adolescents

- prevalence 10% in childhood/adolescence; F:M=2:1
- often not recognized

Clinical Features
- becomes problematic when it interferes with typical academic/social functioning
- children and adolescents may not vocalize their anxiety but instead exhibit behavioural manifestations
- associated with school problems, unrealistic worries, physical/somatic symptoms (abdominal pain, headaches), social and relationship problems, social withdrawal and isolation, sleep difficulties, tearful episodes or temper tantrums, lack of confidence, irritability and mood symptoms, alcohol and drug use in adolescents
- tension may look like fidgeting

Differential Diagnosis
- depressive disorders, ODD, truancy
- persistence and impairment to daily functioning differentiates anxiety disorder from normal anxiety
- for school avoidance, differentiate social anxiety (fear of performance and humiliation) from generalized anxiety
- consider anxiety about separation, and rule out bullying and school refusal due to learning disorder

Course and Prognosis
- better prognosis with later age of onset, fewer comorbidities, early initiation of treatment, ability to maintain school attendance and peer relationships, and absence of social anxiety disorder
- with treatment, up to 80% of children will not meet criteria for their anxiety disorder at 3 yr follow-up, but up to 30% will meet criteria for another psychiatric disorder

Treatment
- similar principles for most childhood anxiety disorders due to overlapping symptomatology and frequent comorbidity
- psychoeducation of child and family
- psychotherapy: CBT has been shown to be effective in children and adolescents with anxiety
- pharmacotherapy: SSRIs can be helpful

SEPARATION ANXIETY DISORDER
- excessive and developmentally inappropriate anxiety on real, threatened, or imagined separation from attachment figures or home, with physical or emotional distress for at least 4 wk
- persistent worry about losing attachment figures or experiencing an untoward event to self; reluctance to go places, be alone, or sleep alone; nightmares involving separation; physical symptoms when separated
- often associated with school refusal, comorbid major depression

SOCIAL ANXIETY DISORDER (SOCIAL PHOBIA)
- anxiety, fear, and/or avoidance provoked by situations where child feels under the scrutiny of others
- must distinguish between shy child, child with issues functioning socially (e.g. autism), and child with social anxiety
  - diagnosis only if anxiety interferes significantly with daily routine, social life, academic functioning, or if markedly distressed. Must occur in settings with peers, not just adults
- features: crying, tantrums, freezing, clinging behaviour, mutism, excessively timid, stays on periphery, refuses to be involved in group play
- significant implication for future quality of life if untreated; lower levels of satisfaction in leisure activities, higher rates of school dropout, poor workplace performance, increased rates of remaining single

SELECTIVE MUTISM
- consistent failure to speak in specific social situations where speaking is expected, despite speaking in other situations for ≥1 mo
- the disturbance interferes with educational or occupational achievement or with social communication
- not due to lack of knowledge of language or communication disorder

GENERALIZED ANXIETY DISORDER
- diagnostic criteria same as adults (note: only 1 item is required in children for Criteria C)
- children worry about many things (e.g. school, future, family, past)
- often redo tasks, show dissatisfaction with their work, and tend to be perfectionistic
- often fearful in multiple settings and expect more negative outcomes when faced with academic or social challenges, and require reassurance and support to take on new tasks

Attachment type can be assessed in infants 10-18 mo of age using the Strange Situation test, in which the child is stressed by the caregiver being removed from the situation and the stranger staying. Attachment style is measured by the child's behaviour during the reunion with the caregiver

Attachment problems may present as a child who is difficult to soothe, has difficulty sleeping, problems feeding, tantrums, or behavioural problems

The shy child is quiet and reluctant to participate but slowly 'warms up'

Fluoxetine, Cognitive-Behavioural Therapy and Their Combination for Adolescents with Depression: Treatment for Adolescents with Depression Study (TADS) Randomized Controlled Trial

JAMA 2004;292:807-820

Purpose: To evaluate effectiveness of fluoxetine alone, cognitive behavioural therapy (CBT) alone, CBT with fluoxetine, and placebo among adolescents with major depressive disorder (MDD).

Methods: Randomized controlled trial at 13 US academic and community clinics between spring 2000-summer 2003, including patients 12-17 y/o with a primary DSM IV diagnosis of MDD assigned to one of the aforementioned four treatment arms. The primary outcome was the Children's Depression Rating Scale-Revised (CDRSR) total score.

Results: Fluoxetine with CBT had a statistically significant CDRSR score as compared to placebo (P=0.001) with a 71% response rate. This combination was greater than fluoxetine alone (P=0.02), and CBT alone (P=0.01). Fluoxetine alone was greater than CBT alone (P=0.01).

Conclusion: Combination of fluoxetine with CBT offered the most favourable benefit-risk tradeoff for adolescents with MDD.

SPECIFIC PHOBIA
- common phobias in childhood: fear of heights, small animals, physicians, dentists, darkness, loud noises, thunder, lightning

OCD
- diagnostic criteria same as adults
- note: young children may not be able to articulate the aims of their compulsions

Neurodevelopmental Disorders

Autism Spectrum Disorder

Diagnosis
- persistent deficits in social communication and interaction, manifested in three areas:
  - **social-emotional reciprocity**: abnormal social approach and failure of normal back-and-forth conversation; reduced sharing of interests, emotions, or affect; failure to initiate or respond to social interactions
  - **nonverbal communicative behaviours**: poorly integrated verbal and nonverbal communication; abnormalities in eye contact and body language or deficits in understanding and use of gestures; total lack of facial expressions and nonverbal communication
  - **developing, maintaining, and understanding relationships**: difficulties adjusting behaviour to suit various social contexts; difficulties in sharing imaginative play or in making friends; absence of interest in peers
- restricted, repetitive patterns of behaviour, interests, or activities manifested by ≥2 of: stereotyped or repetitive motor movements, insistence on sameness, highly restricted fixated interests, hyper-/hypo-reactivity to sensory input
- symptoms must be present in early developmental period
- symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning
- not better explained by intellectual disability or global developmental delay
- **specifiers**
  - current severity: requiring very substantial support, requiring substantial support, requiring support
  - ± language impairment, ± intellectual impairment, ± catatonia
  - associated with known medical or genetic condition or environmental factor

Differential Diagnosis
- neurodevelopmental: global delay, intellectual disability, language disorder, social communication disorder, learning disorder, developmental coordination disorder, stereotypic movement disorder
- mental and behavioural: ADHD, mood disorder, anxiety disorder, selective mutism, attachment disorder, ODD, conduct disorder, OCD, childhood schizophrenia
- conditions with developmental regression: Rett syndrome, epileptic encephalopathy (Landau-Kleffner)
- other: hearing/visual impairment, abuse

Treatment
- team-based: school, psychologist, occupational therapist, physiotherapist, speech-language pathologist, paediatrics, psychiatry
- psychosocial: family education and support, school programming, behavioural therapy, social skills training
- treat concomitant disorders such as ADHD, tics, OCD, anxiety, depression, and seizure disorder
- adjunctive pharmacotherapy (does not treat ASD itself): atypical antipsychotics (for irritability, aggression, agitation, self-mutilation, tics), SSRIs (for anxiety, depression), stimulants (for associated inattention and hyperactivity)

Prognosis
- variable, but improves with early intervention

Attention Deficit Hyperactivity Disorder

- prevalence: 5-12% of school-aged children; M:F=4:1, although girls may be under-diagnosed
- girls tend to have inattentive symptoms; boys tend to have impulsive/hyperactive symptoms

Etiology
- genetic: 75% heritability, dopamine candidate genes DAT1, DRD4
- neurobiology: decreased catecholamine transmission, low prefrontal cortex (PFC) activity, increased β activity on EEG
- cognitive: developmental disability, poor inhibitory control, and other errors of executive function

Efficacy and Safety of Selective Serotonin Reuptake Inhibitors, Serotonin-Norepinephrine Reuptake Inhibitors, and Placebo for Common Psychiatric Disorders Among Children and Adolescents: A Systematic Review and Meta-Analysis

JAMA Psychiatry 2017;74(10):1011-1020

Purpose: Examine the relative efficacy and safety of SSRIs, SNRIs, and placebo for the treatment of depressive disorders (DDs), anxiety disorders (ADs), obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD) in children and adolescents.

Methods: Meta-analysis of RCTs regarding use of SSRIs or SNRIs in youths with DD, AD, OCD, or PTSD. Effect sizes, calculated as standardized mean differences (Hedges g) and risk ratios (RRs) for adverse events, were assessed in a random-effects model.

Results: Thirty-six trials were eligible and analysis showed that SSRIs and SNRIs were more beneficial compared with placebo (g = 0.32; 95% CI, 0.25-0.40; P < .001). ADs (g = 0.56; 95% CI, 0.40-0.72; P < .001) had larger between-group effect sizes than DDs (g = 0.20; 95% CI, 0.13-0.27; P < .001). Patients with DDs exhibited significantly larger placebo responses (g = 1.57; 95% CI, 1.36-1.78; P < .001) compared with those with ADs (g = 1.03; 95% CI, 0.84-1.21; P < .001). The SSRIs produced a relatively large effect size for ADs (g = 0.71; 95% CI, 0.45-0.97; P < .001). Patients receiving an antidepressant vs. a placebo reported significantly more treatment-emergent adverse events (RR, 1.07; 95% CI, 1.01-1.12; P = .01 or RR, 1.49; 95% CI, 1.22-1.82; P < .001, depending on the reporting method), severe adverse events (RR, 1.76; 95% CI, 1.34-2.32; P < .001), and study discontinuation due to adverse events (RR, 1.79; 95% CI, 1.38-2.32; P < .001).

Conclusion: Compared with placebo, SSRIs and SNRIs are more beneficial than placebo in children and adolescents; however, the benefit is small and disorder specific, yielding a larger drug-placebo difference for AD than for other conditions. Response to placebo is large, especially in DD. Severe adverse events are significantly more common with SSRIs and SNRIs than placebo.

Diagnosis

- diagnosis requires: onset before age 12, persistent symptoms ≥6 mo, symptoms present in ≥2 settings (i.e. home, school, work), interferes with academic, family, and social functioning, and is divided into 3 subtypes
  - combined type: ≥6 symptoms of inattention and ≥6 symptoms of hyperactivity-impulsivity
  - predominantly inattentive type: ≥6 symptoms of inattention
  - predominantly hyperactive-impulsive type: ≥6 symptoms of hyperactivity-impulsivity
  - for older adolescents and adults (≥ age 17), ≥5 symptoms required
- does not occur exclusively during the course of another psychiatric disorder
- DDx: learning disorders, hearing/visual defects, thyroid, atopic conditions, congenital problems (fetal alcohol syndrome, Fragile X), lead poisoning, history of head injury, traumatic life events (abuse)
- specify current severity (mild/moderate/severe); if in partial remission (past diagnosis, has not met full criteria >6 mo, still functional impairment present)

Table 13. Core Symptoms of ADHD (DSM-5)

Inattention	Hyperactivity	Impulsivity
Careless mistakes	Fidgets, squirms in seat	Blurts out answers before questions completed
Cannot sustain attention in tasks or play	Leaves seat when expected to remain seated	Difficulty awaiting turn
Does not listen when spoken to directly	Runs and climbs excessively	Interrupts/intrudes on others
Fails to complete tasks	Cannot play quietly	
Disorganized	"On the go", driven by a motor	
Avoids and/or dislikes tasks that require sustained mental effort	Talks excessively	
Loses things necessary for tasks or activities		
Distractible		
Forgetful		

Clinical Features

- difficult to differentiate from highly variable normative behaviour before age 4, but often identified upon school entry
- present across multiple settings - school, home, extracurricular
- rule out developmental delay, sensory impairments, genetic syndromes, encephalopathies, or toxins (alcohol, lead)
- increased risk of substance use disorder, depression, anxiety, academic failure, poor social skills, comorbid CD and/or ODD, adult ASPD
- associated with family history of ADHD, difficult temperamental characteristics

Treatment

- non-pharmacological: psychoeducation, behavioural management (e.g. parent training, classroom management, social skills training)
- pharmacological: 1st line: stimulants (methylphenidate, amphetamines); 2nd line: atomoxetine and guanfacine XR; 3rd line: clonidine, bupropion, imipramine
- for comorbid symptoms: antidepressants, antipsychotics
- psychosocial intervention is first line for children <6, whereas psychosocial intervention plus medication is considered first line for children ≥6

Prognosis

- 70-80% continue into adolescence, but hyperactive symptoms usually abate
- 65% continue into adulthood; secondary personality disorders and compensatory anxiety disorders are identifiable

Comparative Efficacy and Tolerability of Medications for Attention-Deficit Hyperactivity Disorder in Children, Adolescents, and Adults: A Systematic Review and Network Meta-Analysis
Lancet 2018;5:727-738
Purpose: Estimate the comparative efficacy and tolerability of oral medications for ADHD in children, adolescents, and adults.
Methods: Review of double-blind RCTs comparing amphetamines, atomoxetine, bupropion, clonidine, guanfacine, methylphenidate, and modafinil with each other or placebo.
Conclusions: Taking into account both efficacy and safety, evidence from this meta-analysis supports methylphenidate in children and adolescents, and amphetamines in adults, as preferred first-choice medications for the short-term treatment of ADHD.

Contrary to the concerns of many parents and health care providers, treatment with stimulant medications of ADHD in childhood does not increase the likelihood of substance misuse later in life

Disruptive, Impulse Control, and Conduct Disorder

Oppositional Defiant Disorder

- prevalence: 2-16%, M=F after puberty

Diagnosis

- pattern of negativistic/hostile and defiant behaviour for ≥6 mo, with ≥ 1 non-sibling, with ≥4 symptoms manifested in 3 areas of:
  - **angry/irritable mood**: easily loses temper, touchy or easily annoyed, often angry and resentful
  - **argumentative/defiant**: argues with adults/authority figure, defies requests/rules, deliberately annoys, blames others for their own mistakes or misbehaviour
  - **vindictiveness**: spiteful or vindictive twice in past 6 mo
  - **note**: difference between normal behaviour and ODD is frequency of symptoms (most days if age <5 yr, weekly if age ≥5 yr) exceeds what is normative for one's age gender, culture
- behaviour causes significant distress or impairment in social, academic, or occupational functioning
- behaviours do not occur exclusively during the course of a psychotic, substance use, or mood disorder
- severity (mild/moderate/severe) according to number of settings in which symptoms are present
- diagnosis of disruptive mood dysregulation disorder supersedes ODD if criteria for both are met

Clinical Features

- first symptoms usually appear during preschool and rarely later than early adolescence
- associated with poor school performance, few friends, strained parent/child relationships, risk of developing mood disorders later on, often precedes CD

Treatment

- parent: parent management training, psychoeducation for parents and family
- behavioural therapy: to teach, practice, and reinforce prosocial behaviour
- social: school/day-care interventions
- pharmacotherapy for comorbid disorders

Conduct Disorder

- prevalence: 1.5-3.4% (M:F=4:1)

Etiology

- parental/familial factors: parental psychopathology (e.g. ASPD, substance use disorder), child-rearing practices (e.g. child abuse, discipline), low socioeconomic status (SES), family violence
- child factors: difficult temperament, ODD, learning problems, ADHD, neurobiology

Diagnosis

- pattern of behaviour that violates rights of others and age appropriate social norms with ≥3 criteria noted in past 12 mo and ≥1 in past 6 mo:
  - aggression to people and animals: bullying, initiating physical fights, use of weapons, forced sex, cruel to people and/or animals, stealing while confronting a person (i.e. armed robbery)
  - destruction of property: arson, deliberately destroying others' property
  - deceitfulness or theft: breaking and entering, conning others, stealing nontrivial items without confrontation
  - violation of rules: out all night before age 13, often truant from school before age 13, runaway ≥2 times at least overnight or for long periods of time
  - disturbance causes clinically significant impairment in social, academic, or occupational functioning
  - if ≥18 yr, criteria not met for ASPD
- diagnostic types
  - childhood-onset (≥1 criterion prior to age 10)
  - adolescent-onset (no criteria until age 10)
  - unspecified onset (insufficient information)
  - mild, moderate, severe
- differential: ADHD, depression, head injury, substance misuse

Treatment

- early intervention necessary and more effective; long-term follow-up required
- psychosocial: parent management training, anger replacement training, CBT, family therapy, education/employment programs, social skills training
- pharmacotherapy for comorbid disorders

Children with ODD like "RATs and BEARS"

Rule breaker
Annoying
Temper

Blames others
Easily annoyed
Argues with adults
Resentful
Spiteful/vindictive

A Systematic Review and Analysis of Long-Term Outcomes in Attention Deficit Hyperactivity Disorder: Effects of Treatment and Non-Treatment
BMC Med 2012;10:99
Purpose: To determine the long-term outcomes of ADHD and whether there is an effect on long-term outcomes with treatment.
Methods: Systematic review of studies, including patients with diagnosed or symptomatic presentation of ADHD, assigned to pharmacological, non-pharmacological, multi-modal treatments, or a no-treatment control. Outcome measures included use/addictive behaviour, academic outcomes, antisocial behaviour, social function, occupation, self-esteem, driving outcomes, services use, and obesity.
Results: Untreated participants with ADHD had poorer outcomes vs. non-ADHD participants in 74% (n=244) of studies, while 26% (n=89) showed similar outcomes. 72% (n=37) of studies showed a benefit from ADHD treatment vs. untreated ADHD and 28% (n=15) showed no benefit. Treatment of ADHD was found to be beneficial in studies looking at driving (100%), obesity (100%), self-esteem (90%), social function (83%), academic outcomes (71%), drug use/addictive behaviour (67%), antisocial behaviour (50%), and occupation (33%).
Conclusion: Overall, people with ADHD have poorer long-term outcomes than controls (those without ADHD). For those with ADHD, treatment improves long-term outcomes.

Conduct Disorder Diagnosis

TRAP
Theft: breaking and entering, deceiving, non-confrontational stealing
Rule breaking: running away, skipping school, out late
Aggression: people, animals, weapons, forced sex
Property destruction

Prognosis
- poor prognostic indicators include: early-age onset, high frequency, variety of behaviours, pervasiveness (i.e. in home, school, community), comorbid ADHD, early sexual activity, substance misuse
- 50% of children with CD develop ASPD as adults

Intermittent Explosive Disorder

Diagnosis
- recurrent behavioural outbursts representing a failure to control aggressive impulses in children ages ≥6, manifested as either:
  - verbal or physical aggression that does not damage others or property, occurring ≥2 times per wk for 3 mo
  - 3 outbursts involving physical damage to another person, animal, or piece of property in the last 12 mo
- outbursts are out of proportion to triggers and are not premeditated/for primary gain
- outbursts cause clinically significant distress or impairment in occupation or interpersonal functioning, or financial/legal consequences

See Paediatrics
- *Child Abuse*, P18, *Chronic Abdominal Pain*, P48, *Developmental Delay*, P26, *Intellectual Disability*, P27, Learning Disabilities, P29, *Sleep Disturbances*, P15

See Neurology
- *Tic Disorders*, N35, *Tourette's Syndrome*, N35

Psychotherapy

- treatment in which a person with mental or physical difficulties aims to achieve symptomatic relief through interactions with another person
- psychotherapy is delivered by a trained counsellor, social worker, nurse, psychologist, general practitioner, or psychiatrist
- various types of therapy exist based on diverse theories of human psychology and mental illness etiology

Freud's Personality Theory – Three Parts of the "Psyche"
- **id**: instinctual drives, unconscious
- **superego**: person's conscience, formed by societal/parental norms
- **ego**: Latin "I", sense of self, conscious actions, attempts to satisfy drives of id within confines of reality and demands of superego

Common Factors of Psychotherapy
- good evidence that effective psychotherapy creates observable changes in brain circuitry and connectivity, but these changes are different from those observed with successful pharmacologic and other treatment modalities
- studies suggest that up to 60-90% of therapy outcome is due to common factors with only 10-40% due to specific factors
- common factors are warmth (unconditional positive regard), accurate empathy, genuineness, goodness of fit, relationship with provider predicts positive outcomes

Table 14. Summary of Psychotherapeutic Modalities

Type	Indications	Approach, Technique, and Theory	Ideal Candidates	Duration
Supportive Therapy	Adjustment disorders, somatic symptoms and related disorders, severe psychotic or personality disorders Adjunct to pharmacologic management in most disorders	Uses empathy, validation, and reflection to facilitate adaptation and coping Help patients feel safe, secure, and encouraged	Individuals in crisis or with severe symptoms in acute or chronic settings	Variable (single session to years, though often short-intermittent)
Interpersonal Therapy	Mood disorders	Focuses on how interpersonal relationships impact symptoms 4 key problem areas addressed: 1. grief and loss, 2. role transitions, 3. conflict, 4. interpersonal deficits Break the interpersonal cycle: depression, self-esteem, social withdrawal	Individuals with depression or bipolar disorder with some insight and difficult social functioning Absence of severe psychotic process, personality disorder, or comorbid substance use disorder	Weekly sessions, 12-20 sessions
Cognitive Behavioural Therapy	Most mental health disorders including: mood, anxiety, OCD, personality, eating, substance use, psychotic disorders	Combines theory and method from cognitive and behavioural therapies to teach the patient to change connections between thinking patterns, habitual behaviours, and mood/anxiety problems Cognitive component includes using thought records to help monitor thoughts and identify inaccurate automatic thoughts Behavioural component includes techniques such as systematic desensitization (mastering anxiety-provoking situations by approaching them gradually and in a relaxed state that limits anxiety), flooding (confronting feared stimulus for prolonged periods until it is no longer frightening), positive reinforcement (strengthening behaviour and causing it to occur more frequently by rewarding it), negative reinforcement (causing behaviour to occur more frequently by removing a noxious stimulus when desired behaviour occurs), extinction (causing a behaviour to diminish by not rewarding it), and punishment/aversion therapy (causing a behaviour to diminish by applying a noxious stimulus)	Individuals with motivation to change and who are able to participate in homework	Typically weekly or twice weekly sessions, 12-20 sessions Maintenance therapy can be carried out over years
Dialectical Behavioural Therapy	Borderline personality disorder	Therapy that combines CBT techniques with Buddhist Zen mindfulness practices and dialectical philosophy Focuses on 4 types of skills: mindfulness, emotional regulation, interpersonal effectiveness, and distress tolerance Involves 4 components: individual therapy, group skills training, phone consultations, and a consultation team	Individuals with borderline personality disorder or borderline personality trait and severe problems of emotional dysregulation, impulsivity, or self-harm	Typically 1 yr Weekly individual and group therapy
Motivational Interviewing and Motivational Enhancement herapy	Substance use disorders Techniques can be applied to facilitate behavioural change in most psychological problems	Spirit of MI (CAPE): Compassion, Acceptance, Partnership, Evocation Principles of MI (RULE): Resist "righting reflex", Understand client and their reasons for change, Listen, Empower by conveying hope and supporting autonomy Techniques of MI (OARS): Open-ended questions, Affirmations to validate client, Reflections (the skill of accurate empathy), Summaries to help client organize self	Individuals with problematic substance use, maladaptive behaviour patterns (therapy disengagement, medication noncompliance, poor health habits)	Brief interventions (efficacy with as little as 15 min, single session), better result with more sessions Addiction is a chronic condition, often need boosters over time MET = 4 sessions
Group Psychotherapy	Most mental health disorders including mood, anxiety, OCD, personality, eating, substance use, and psychotic disorders can benefit from group therapy as part of treatment	Aims to promote self-understanding, acceptance, social skills	Adolescents, individuals not currently in crisis, absence of severe psychotic symptoms	Variable Often time-limited (e.g. weekly sessions for 12 wk)
Family Therapy	Most mental health disorders including mood, anxiety, OCD, personality, eating, substance use, and psychotic disorders can benefit from group therapy as part of treatment	Family system considered more influential than individual, especially for children Focus on here and now, re-establishing parental authority, strengthening normal boundaries, and rearranging alliances	Children and adolescents with families willing to engage in treatment	Often short-term (e.g. 12 sessions)
Mindfulness-based Cognitive Therapy/ Mindfulness-based Stress Reduction	Emerging evidence for treating adjustment disorder, MDD (relapse prevention), anxiety, pain disorders, insomnia, substance use disorder (relapse prevention)	Derived from Buddhist meditative and philosophical practices; aims to help people attend to thoughts, behaviours, and emotions in the moment and non-judgmentally using guided breathing exercises	Individuals who are motivated and willing to engage in therapy	Generally weekly sessions for 8 wk
Psychoanalytic/ Psychodynamic Therapy	Anxiety, obsessional thinking, conversion disorder, depression	Theory: exploration of meaning of early experiences and how they affect emotions and patterns of behaviour Recollection (remembering), repetition (reliving with the therapist), working through (gaining insight) Techniques: free association, dream interpretation, transference analysis	Psychologically minded, highly motivated, wish to understand selves and not just relieve symptoms Able to withstand difficult emotions without fleeing or self-destructive acts High level of function	Time intensive: Psychoanalysis: 4-5 times/wk for 3-7 yr Psychodynamically oriented therapy: 2-3 times/wk for fewer yr

Pharmacotherapy

Antipsychotics

- "antipsychotics" used to be called "neuroleptics"
- overall mechanism of action: functionally antagonize, to varying degrees, D2 activity in target brain pathways
- primarily indicated for psychotic symptoms in: schizophrenia and related disorders, manic episodes, depressive episodes, substance use, medical conditions (e.g. neoplasm)
- other uses: treatment-resistant MDD, severe GAD, complex PTSD, severe OCD, borderline PD, behavioural symptoms of dementia, delirium, Tourette syndrome, substance use disorder in dual diagnosis, Huntington's disease, ASD, and impulse control disorders
  - adjunctive management of agitation, aggression, severe anxiety, and severe sleep difficulties when sedative-hypnotics are contraindicated
- onset: acute, rapid calming effect and decrease in agitation; the antipsychotic effect with improvement in thought disorder, delusions, and hallucinations may take 1-4 wk
- rational use
  - no reason to combine two or more antipsychotics, although this is quite common in clinical practice
  - all antipsychotics are equally effective, except for clozapine (considered to be most effective in treatment-resistant schizophrenia)
  - atypical antipsychotics (i.e. second generation) are as effective as typical (i.e. first generation) antipsychotics but are thought to have better adverse effect profiles; main difference is lower risk of EPS and TD but more metabolic side effects (see sidebar)
  - choose a drug to which the patient has responded to in the past or that was used successfully in a family member
- route: PO, short-acting or long-acting depot IM injections, and sublingual; more recently there is inhaled loxapine mainly for use in acute agitation
- if no response in 4-6 wk, switch drugs
- duration: minimum 6 mo and usually for life in most patients with primary psychotic disorders; variable for other indications

Long-Acting Preparations

- antipsychotics formulated in oil for IM injection
- received on an outpatient basis
- indications: initially meant for individuals with schizophrenia or other chronic psychosis who relapse because of non-adherence, but current initial evidence suggests they are better than oral preparations overall
- should have been exposed to oral form prior to first injection
- dosing: start at low dosages, then titrate every 2-4 wk to maximize safety and minimize side effects
- side effects: similar to side effect profile to oral preparation of the same drug

Canadian Guidelines for the Treatment of Acute Psychosis in the Emergency Setting

- haloperidol 5 mg IM ± lorazepam 2 mg IM
- loxapine PO or IM 25 mg ± lorazepam 2 mg IM
- olanzapine 2.5-10 mg (PO, IM, oral quick dissolve – its time to peak is the same as regular PO)
- risperidone 2 mg (M-tab, liquid)

Dopamine Pathways Affected by Antipsychotics

Pathway	Effects	Associated Pathology
Mesolimbic	Emotion origination, reward	HIGH dopamine causes positive symptoms of schizophrenia (delusions, hallucinations)
Mesocortical	Cognition, executive function	LOW dopamine causes negative symptoms of schizophrenia
Nigrostriatal	Movement	LOW dopamine causes EPS
Tubero-infundibular	Prolactin hormone release	LOW dopamine causes hyper-prolactinemia

Typical (First Generation) vs. Atypical (Second Generation) Antipsychotics

	Typical	Atypical
Mechanism	Block postsynaptic dopamine receptors (D2)	Block postsynaptic dopamine receptors (D2) Block serotonin receptors (5-HT2) on presynaptic dopaminergic terminals, triggering DA release, and reversing DA blockade in some pathways. Some are partial D2 agonists
Pros	Inexpensive Plenty of injectable forms available	EPS less prevalent Low-risk of tardive syndromes Mood stabilizing effects
Cons	EPS more prevalent, including tardive syndromes in long-term Not mood stabilizing	Expensive Few injectable forms available Metabolic side effects (weight gain, hyperglycemia, lipid abnormalities, metabolic syndrome) Exacerbation (or new onset) of obsessive behaviour

Anticholinergic Effects

Red	as a	beet
Hot	as a	hare
Dry	as a	bone
Blind	as a	bat
Mad	as a	hatter

Table 15. Common Antipsychotic Agents

	Starting Dose	Maintenance	Maximum	Relative Potency (mg)
Typicals (in order of potency from high to low)				
Haloperidol (Haldol®)	2-5 mg IM q4-8 h 0.5-5 mg PO B/TID 0.2 mg/kg/d PO	Based on clinical effect	20 mg/d PO	2
Fluphenazine enanthate (Moditen®, Modecate® for IM formulation)	2.5-10 mg/d PO	1-5 mg PO QHS 25 mg IM/SC q1-3 wk	20 mg/d PO	2
Zuclopenthixol HCl (Clopixol®)	20-30 mg/d PO	20-40 mg/d PO	100 mg/d PO	4
Zuclopenthixol acetate (Acuphase®)	50-150 mg IM q48-72 h		400 mg IM (q2 wk)	
Zuclopenthixol decanoate (Cloxipol Depot®)	100 mg IM q1-4 wk	150-300 mg IM q2 wk	600 mg IM/wk	
Perphenazine (Trilafon®)	8-16 mg PO B/TID	4-8 mg PO T/QID	64 mg/d PO	10
Loxapine HCl (Loxitane®)	10 mg PO TID 12.5-50 mg IM q4-6 h	60-100 mg/d PO	250 mg/d PO	10
Chlorpromazine (Largactil®)	10-25 mg PO B/T/QID	400 mg/d PO	1000 mg/d PO	100
Atypicals (in order of potency from high to low)				
Risperidone (Risperdal®, Risperdal Consta® for IM long acting preparation, Risperdal® M-Tab for melting form – placed on tongue)	1-2 mg once daily/BID	4-8 mg/d PO 25 mg IM q2 wk	8 mg/d PO	2
Paliperidone (Invega®, Invega Sustenna® (one v) or Trinza® (three months) for IM long acting preparations)	3 mg/d PO	3-12 mg /d PO	12 mg/d PO	4
Olanzapine (Zyprexa®, Zyprexa Zydis® for melting form – placed on tongue)	5 mg/d PO	10-20 mg/d PO	30 mg/d PO	5
Asenapine (Saphris®)	5 mg SL BID	5-10 mg SL BID	10 mg SL BID	5
Ziprasidone (Zeldox®)	20 mg PO BID	40-80 mg PO BID	160 mg/d PO	6
Aripiprazole (Abilify®)	10-15 mg/d PO	10-15 mg/d PO	30 mg/d PO	7.5
Quetiapine (Seroquel®, Seroquel XR® for extended release®)	25 mg PO BID	400-800 mg/d PO	800 mg/d PO	75
Clozapine (Clozaril®)	25 mg PO BID	300-600 mg/d PO	900 mg/d PO	100

See Landmark Psychiatry Trials table for more information on CATIE, which details a comparison between first and second-generation antipsychotics in the treatment of schizophrenia.

Metabolic and Cardiovascular Adverse Effects Associated with Antipsychotic Drugs
Nat Rev Endocrinol 2012;8:114-126
All atypical antipsychotics can cause cardiovascular and metabolic side effects, such as obesity, dyslipidemia, hyperglycemia, and weight gain. Olanzapine and clozapine are most likely to cause these adverse effects. The mechanism that underlies the metabolic and cardiovascular effects is not fully understood. However, the histamine, dopamine, serotonin, and muscarinic receptors are implicated.

QTc prolongation is an important adverse effect of all antipsychotics; although not required, consider getting ECG prior to and after initiating new medication and to monitor QTc
Typicals: chlorpromazine and haloperidol warrant systematic baseline and follow-up ECG
Atypicals: ziprasidone has the highest risk among atypicals, clozapine also warrants systematic baseline and follow-up ECG

Features of Neuroleptic Malignant Syndrome

FARM
Fever
Autonomic changes (e.g. increased HR/BP, sweating)
Rigidity of muscles
Mental status changes (e.g. confusion)

FARM symptoms are also seen in serotonin syndrome (SS)
SS can be distinguished from NMS by the following:

SS	NMS
Twitchy, shivering, restless	Severe global rigidity
Flushed, sweaty	Pallor
Vomiting, diarrhea, abdominal pain	No GI symptoms

Table 16. Commonly Used Atypical Antipsychotics

	Risperidone (Risperdal®) / Paliperidone (Invega®)	Olanzapine (Zyprexa®, Zydis®)	Quetiapine (Seroquel®)	Clozapine (Clozaril®)	Aripiprazole (Abilify®)
Advantages	Lower incidence of EPS than typical antipsychotics at lower doses (<8 mg) Associated with less weight gain compared to clozapine and olanzapine	Better overall efficacy compared to haloperidol Well tolerated Low incidence of EPS and TD	Associated with slightly less weight gain compared to clozapine and olanzapine, but more than the other atypicals Mood stabilizing	Most effective for treatment-resistant schizophrenia Does not worsen tardive symptoms; may treat them Approximately 50% of patients benefit, especially paranoid patients and those with onset after 20 yr	Less weight gain and risk of metabolic syndrome compared to olanzapine and a lower incidence of EPS compared to haloperidol Mood stabilizing
Disadvantages relative to other SGAs	Highest risk of EPS/TD among SGAs – avoid if high-risk for EPS or existing movement disorder or elderly Elevated prolactin - sexual dysfunction, galactorrhea, gynecomastia, menstrual disturbance, infertility	Weight gain and metabolic effects – avoid in DM Sedating – avoid if high-risk for falls or fracture	Sedating/orthostatic hypotension – avoid if high-risk for falls or fracture QT prolongation in high doses – caution if cardiac risk	Weight gain and metabolic effects- avoid in DM Sedating/orthostatic hypotension - avoid if high-risk for falls or fracture Potentially severe constipation - avoid if risk of fecal impaction or bowel perforation Cardiomyopathy – caution if existing heart disease Reduces seizure threshold - caution if seizure disorder Agranulocytosis (1%) – avoid in existing leukopenia/ neutropenia, requires ongoing CBC monitoring	Insomnia, akathisia
Comments	Quick dissolve (M-tabs), and long-acting (Consta®/ Invega Trinza®) formulations available	Quick dissolve formulation (Zydis®) used commonly in ER setting for better compliance (but does not act faster) Acute IM form available		Weekly blood counts for 6 mo, then q2 wk Do not use with other drugs that may cause bone marrow suppression due to risk of agranulocytosis	

Note: Risk of weight gain: Clozapine > Olanzapine > Quetiapine > Risperidone

Table 17. Side Effects of Antipsychotics

System	Side Effects
Anticholinergic	Dry mouth, urinary retention, constipation, blurred vision, confusional states
α-adrenergic Blockade	Orthostatic hypotension, erectile dysfunction, failure to ejaculate
Dopaminergic Blockade	Extrapyramidal syndromes, galactorrhea, amenorrhea, erectile dysfunction, weight gain
Anti-Histamine	Sedation, weight gain
Hematologic	Agranulocytosis (clozapine)
Hypersensitivity Reactions	Liver dysfunction, blood dyscrasias, skin rashes, neuroleptic malignant syndrome, altered temperature regulation (hypothermia or hyperthermia)
Endocrine	Metabolic syndrome
Cardiac	QT prolongation

Neuroleptic Malignant Syndrome

- psychiatric emergency
  - hypothesis: due to strong DA blockade; increased incidence with high potency and depot antipsychotics
- risk factors
  - medication factors: sudden increase in dosage, starting a new drug
  - patient factors: medical illness, dehydration, exhaustion, poor nutrition, external heat load, male, young adults
- clinical features
  - tetrad: mental status changes (usually occur first), fever, rigidity, autonomic instability
  - develops over 24-72 h
  - labs: increased creatine phosphokinase, leukocytosis, myoglobinuria
- treatment: supportive - discontinue antipsychotic drug, hydration, cooling blankets, dantrolene (hydantoin derivative, used as a muscle relaxant), bromocriptine (DA agonist)
- mortality: 5%

Extrapyramidal Symptoms

- incidence related to increased dose and potency
- acute (early-onset; reversible) vs. tardive (late-onset; often irreversible)

Table 18. Extrapyramidal Symptoms

	Dystonia	Akathisia	Parkinsonism	Dyskinesia
Acute or Tardive	Both	Both	Acute	Tardive
High-Risk Groups	Acute: young Asian and Black males	Older females	Older females	Older patients
Presentation	Sustained abnormal posture; torsions, twisting, contraction of muscle groups; muscle spasms (i.e. oculogyric crisis, laryngospasm, torticollis)	Motor restlessness; crawling sensation in legs relieved by walking; very distressing, increased risk of suicide and poor adherence	Tremor; rigidity (cogwheeling); akinesia; postural instability (decreased/absent arm-swing, stooped posture, shuffling gait, difficulty pivoting)	Purposeless, involuntary, constant movements that involve facial and mouth musculature; less commonly – the limbs; rarely, the diaphragm ("hiccups")
Onset	Acute: within 5 d Tardive: >90 d	Acute: within 10 d Tardive: >90 d	Acute: within 30 d	Tardive: >90 d, more commonly yr
Treatment	Acute: benztropine or diphenhydramine, usually IM	Acute: lorazepam, propranolol, benztropine, or diphenhydramine; best approach: reduce dose or change antipsychotic to lower potency	Acute: benztropine; reduce dosage or change antipsychotic to low potency atypical antipsychotic	Tardive: no good treatment; may try clozapine; discontinue drug or reduce dosage Recently the FDA approved valbenazine and deutetrabenazine for the treatment of tardive dyskinesia

Anticholinergic Agents

- types
  - benztropine (Cogentin®) 2 mg PO, IM, or IV once daily (1-6 mg)
  - diphenhydramine (Benadryl®) 25-50 mg PO/IM QID
- do not routinely prescribe with antipsychotics
  - give anticholinergic agents only if at high-risk for acute EPS or if acute EPS develops
- do not give these for tardive syndromes because they worsen the condition

Antidepressants

- onset of effect
  - relief of neuro-vegetative/physical symptoms: 1-3 wk
  - relief of emotional/cognitive symptoms: 2-6 wk
- tapering of most antidepressants is usually required to avoid withdrawal reactions; speed of taper is based on the medication's half-life and the patient's individual sensitivity (i.e. fluoxetine does not require a taper due to its long half-life; paroxetine and venlafaxine require a slower taper than sertraline or citalopram)
- must be vigilant over the first 2 wk of therapy; neuro-vegetative symptoms may start to resolve while emotional and cognitive symptoms may not (patients may be at risk for suicidal behaviour during this time, particularly in children/adolescents)
- treatment of bipolar depression
- patients with bipolar disorder (bipolar depression) should not be treated with an antidepressant as the first line treatment
  - patients with bipolar disorder should only be treated with an antidepressant if combined with a mood stabilizer or antipsychotic; monotherapy with antidepressants is not advisable as the depression can switch to mania
  - maintenance of patients with bipolar disorder with antidepressants is not advisable except in specific cases

Comparative Efficacy and Acceptability of 21 Antidepressant Drugs for the Acute Treatment of Adults with Major Depressive Disorder: A Systematic Review and Network Meta-Analysis
Lancet 2018;391:1357-1366
Purpose: Update of literature to compare and rank antidepressants for the acute treatment of adults with unipolar major depressive disorder (MDD).
Methods: Systematic review and network meta-analysis of RCTs.
Results: 522 trials were identified comprising 116477 participants. All antidepressants were more effective than placebo, with ORs ranging between 2.13 (95% credible interval (CrI) 1.89-2.41) for amitriptyline and 1.37 (1.16-1.63) for reboxetine. For acceptability, only agomelatine (OR 0.84, 95% CrI 0.72-0.97) and fluoxetine (0.88, 0.80-0.96) were associated with fewer dropouts than placebo, whereas clomipramine was worse than placebo (1.30, 1.01-1.68). When all trials were considered, differences in ORs between antidepressants ranged from 1.15 to 1.55 for efficacy and from 0.64 to 0.83 for acceptability. In head-to-head studies, agomelatine, amitriptyline, escitalopram, mirtazapine, paroxetine, venlafaxine, and vortioxetine were more effective than other antidepressants (range of ORs 1.19-1.96), whereas fluoxetine, fluvoxamine, reboxetine, and trazodone were the least efficacious drugs (0.51-0.84). For acceptability, agomelatine, citalopram, escitalopram, fluoxetine, sertraline, and vortioxetine were more tolerable than other antidepressants (range of ORs 0.43-0.77), whereas amitriptyline, clomipramine, duloxetine, fluvoxamine, reboxetine, trazodone, and venlafaxine had the highest dropout rates (1.30-2.32), 46 (9%).
Conclusion: All antidepressants were more efficacious than placebo in adults with MDD. Smaller differences between active drugs were found when placebo-controlled trials were included in the analysis.

Table 19. Common Antidepressants

Class	Drug	Daily Starting Dose (mg)*	Therapeutic Dose (mg)	Comments
SSRI	fluoxetine (Prozac®) fluvoxamine (Luvox®) paroxetine (Paxil®) sertraline (Zoloft®) citalopram (Celexa®) escitalopram (Cipralex®)	20 50-100 10 50 20 10	20-80 150-300 20-60 50-200 20-40 10-20	Useful for typical and atypical depression, seasonal depression, anxiety disorders, OCD, eating disorders All SSRIs have similar effectiveness but consider side effect profiles and half-lives Citalopram and escitalopram have the fewest drug interactions and are sleep-wake neutral Sertraline is the safest SSRI in pregnancy and breastfeeding Fluoxetine is the most activating SSRI (recommend taking in the AM) Fluoxetine does not require a taper due to long half-life and is the most used in children and adolescents as it has most evidence Fluvoxamine is sedating (should be taken in PM) and can be involved in many drug-drug interactions For OCD, aim for maximum doses, sometimes higher
SNRI	venlafaxine (Effexor®) desvenlafaxine (Pristiq®) duloxetine (Cymbalta®)	37.5-75 50 30	75-225 50-100 30-60	Useful for depression, anxiety disorders, neuropathic pain
NDRI	bupropion (Wellbutrin®)	100	300-450	Useful for depression, seasonal depression; not recommended for anxiety disorder treatment because of stimulating effects Causes less sexual dysfunction (may reverse effects of SSRIs/SNRIs), weight gain, and sedation Increased risk of seizures at higher doses Contraindicated with history of seizure, stroke, brain tumour, brain injury, closed head injury Important to specify formulation, as available in IR, SR, XL (longest)
TCA (3° Amines)	amitriptyline (Elavil®) imipramine (Tofranil®) clomipramine (Anafranil®)	25-50 25-50 25-50	150-300 150-300 100-250	Useful for OCD (clomipramine is gold standard), melancholic depression, can also be used in other types of depression and anxiety disorders Requires ECG monitoring Check blood levels if using higher dosage Highly lethal in overdose
TCA (2° Amines)	nortriptyline (Aventyl®) desipramine (Norpramin®)	25-50 25-50	75-150 150-300	Preferred to tertiary amines because of lower propensity for anticholinergic adverse effects Requires ECG monitoring Check blood levels if using higher dosage Highly lethal in overdose
MAOI	phenelzine (Nardil®) tranylcypromine (Parnate®)	15 20	60-90 10-60	Useful for moderate/severe depression that does not respond to other antidepressants; atypical depression; anxiety disorders Requires strict adherence to MAOI diet, (low tyramine)
RIMA	moclobemide (Manerix®)	300	300-600	Useful for some anxiety disorders (e.g. social phobia) and depression
NaSSA	mirtazapine (Remeron®)	15	15-45	Useful in depression with prominent features of insomnia, agitation, or cachexia
SPARI	vilazodone (Viibryd®)	10	10-40	Useful in those with constipation as diarrhea is a common side effect
Serotonin Receptor Modulator	vortioxetine (Trintellix®)	5	5-20	May improve cognitive function

*for depression (start with ½ this dose for treatment of anxiety disorders)
MAOI = monoamine oxidase inhibitors; NaSSA = noradrenergic and specific serotonergic agent; NDRI = norepinephrine and dopamine reuptake inhibitors; RIMA = reversible inhibition of MAO-A; SNRI = serotonin and norepinephrine reuptake inhibitors; SSRI = selective serotonin reuptake inhibitors; TCA = tricyclic antidepressants; SPARI = serotonin partial agonist and reuptake inhibitor

Treatment Approach for Depression

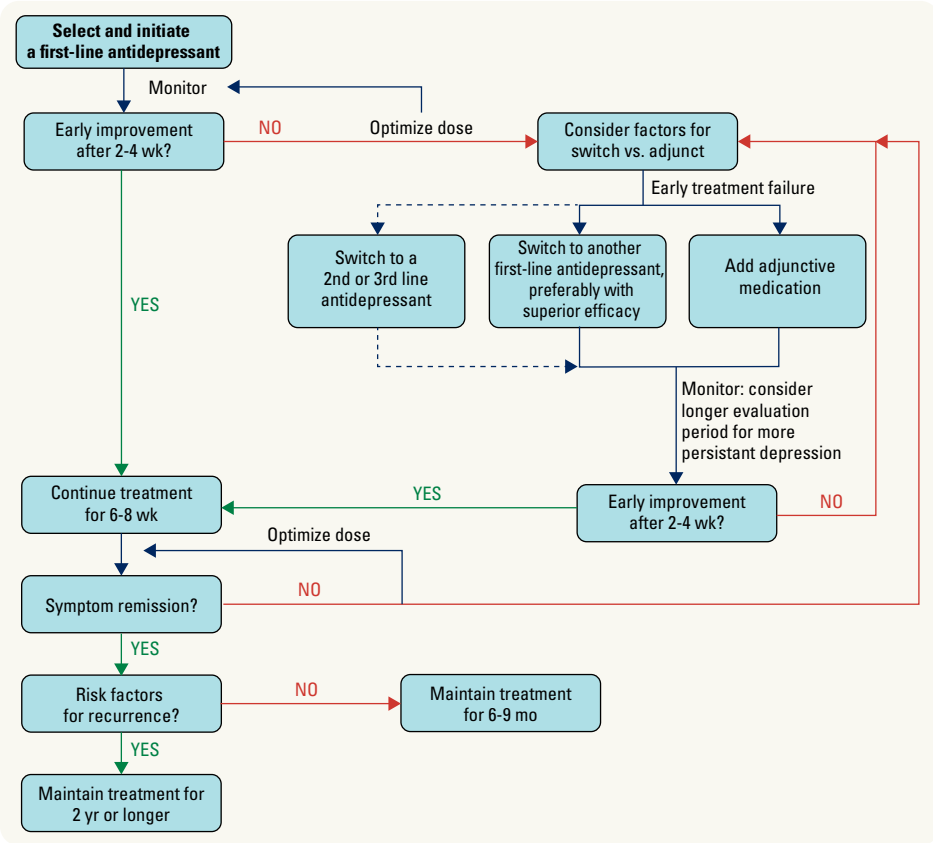

Figure 3. Depression treatment algorithm
Adapted from: Sidney H. Kennedy, Raymond W. Lam, Roger S. McIntyre, et al, The Canadian Journal of Psychiatry (61, 9), p. 21, copyright © 2020, Modified by Permission of SAGE Publications, Inc.

Psychopharmacology of SSRIs

Post-Synaptic Serotonin Receptor Stimulated	Effect/Side Effect
5HT1A centrally	Relief of depression Anxiolytic effect
5HT2A in spinal cord	Sexual dysfunction: delayed ejaculation, anorgasmia, decreased interest/ libido
5HT2C/5HT2A in brain	Activation: anxiety, insomnia Worst with fluoxetine, paroxetine Warn patients anxiety may worsen in first 1-2 wk of treatment
5HT3A in gut	GI upset: nausea, vomiting, bloating Take with food

- **optimization**: increase dosage to maximum tolerated or highest therapeutic dosage
- **augmentation**: the addition of a medication that is not considered an antidepressant to an antidepressant regimen (i.e. thyroid hormone, lithium, atypical antipsychotics (aripiprazole, quetiapine, olanzapine, risperidone))
- **combination**: the addition of another antidepressant to an existing treatment regimen (i.e. the addition of bupropion or mirtazapine to an SSRI or SNRI)
- **switch**: change of the primary antidepressant (within or outside a class)
- note: it is important to fully treat depression symptoms (i.e. to remission) to decrease relapse rates

Symptoms of Antidepressant Discontinuation (mainly from serotonin reuptake inhibition activity)

FINISH
Flu-like symptoms
Insomnia
Nausea
Imbalance
Sensory disturbances
Hyperarousal (anxiety/agitation)

Serotonin Syndrome

- thought to be due to over-stimulation of the serotonergic system
- can result from medication combinations such as more than one SSRI, SSRI + SNRI, SSRI or SNRI + MAOI, SSRI + tryptophan, MAOI + meperidine, MAOI + tryptophan
- rare but potentially life-threatening adverse reaction to SSRIs and SNRIs
- symptoms include: nausea, diarrhea, palpitations, chills, diaphoresis, restlessness, confusion, and lethargy but can progress to myoclonus, hyperthermia, rigor, and hypertonicity
- treatment: discontinue medication and administer emergency medical care as needed
- important to distinguish from NMS

Discontinuation Syndrome

- caused by the abrupt cessation of some antidepressants; most commonly with paroxetine, fluvoxamine, and venlafaxine (drugs with shortest half-lives)
- symptoms usually begin within 1-3 d and can include anxiety, insomnia, irritability, mood lability, N/V, dizziness, headache, dystonia, tremor, chills, fatigue, lethargy, and myalgia ("flu-like symptoms")
- treatment: symptoms may last between 1-3 wk, but can be relieved within 24 h by restarting antidepressant at the same dosage the patient was taking initially and initiating a slower taper over several weeks
- consider avoiding drugs with a short half-life

Table 20. Features of Commonly Used Antidepressant Classes

	SSRI	SNRI	TCA	MAOI	NDRI	RIMA	NaSSA	SPARI	Serotonin receptor modulator
Examples	fluoxetine, sertraline, citalopram	venlafaxine, duloxetine	amitriptyline, clomipramine	phenelzine	bupropion	moclobemide	mirtazapine	vilazodone	vortioxetine
Mode of Action	Block serotonin reuptake only	Block norepinephrine and serotonin reuptake	Block norepinephrine reuptake (clomipramine also blocks serotonin reuptake)	Irreversible inhibition of MAO A and B increases duration that NE, dopamine, and 5HT are in the synaptic cleft by preventing their degradation	Block norepinephrine and dopamine reuptake	Reversible inhibitor of monoamine oxidase A leads to increased duration of norepinephrine, dopamine, and 5HT in the synaptic cleft by preventing their degradation	Enhance central noradrenergic and serotonergic activity by inhibiting presynaptic α-2 adrenergic receptors	5HT1A partial agonism causes downregulation of presynaptic 5HT1A receptors to disinhibit serotonin release, and 5HT4 agonism treats constipation	5HT1A agonism downregulates presynaptic 5HT1A receptors to disinhibit serotonin release, and 5HT7 antagonism theoretically enhances cognitive function
Side Effects	CNS: restlessness, tremor, insomnia, headache, drowsiness, EPS GI: N/V, diarrhea, abdominal cramps, weight gain Sexual dysfunction: erectile dysfunction, anorgasmia CVS: increased HR, increased QTc, serotonin syndrome, SIADH, decreased platelet aggregation – increased risk of bleeding	Low dose side effects similar to SSRIs (serotonergic) Higher dose side effects: tremors, tachycardia, sweating, insomnia, orthostatic hypotension, increase in BP (noradrenergic) SIADH	Anticholinergic effects: (see Table 17, PS54) Noradrenergic effects: tremors, tachycardia, sweating α-1 adrenergic effects: orthostatic hypotension, falls QRS prolongation	Antihistamine effects (minimal): sedation, weight gain CVS: orthostatic hypotension, hypertensive crises with tyramine rich foods (e.g. wine, cheese), or combination with serotonergic or adrenergic medications, headache, flushes, reflex tachycardia, postural hypotension, insomnia Minimal anticholinergic effects	CNS: dizziness, headache, tremor, insomnia, agitation, anxiety, lower seizure threshold CVS: dysrhythmia, HTN GI: dry mouth, N/V, constipation, decreased appetite	CNS (usually minor): dizziness, headache, tremor, insomnia CVS: dysrhythmia, hypotension GI: dry mouth, N/V, diarrhea, abdominal pain, dyspepsia GU: delayed ejaculation Other: diaphoresis	CNS: sedation, dizziness Endocrine: increase in cholesterol, increase in triglycerides, weight gain GI: constipation, ALT elevation	CNS: sedation GI: nausea, diarrhea	GI: nausea
Risk in Overdose	Relatively safe in overdose	Tachycardia and N/V seen in acute overdose	Toxic in overdose 3 times therapeutic dose may be lethal Presentation: anticholinergic effects, CNS stimulation, then depression and seizures ECG: prolonged QRS and QTc (reflect severity) Treatment: activated charcoal, cathartics, supportive treatment, IV diazepam for seizure, physostigmine salicylate for coma Do not give ipecac, as can cause rapid neurologic deterioration and seizures	Toxic in overdose, but wider margin of safety than TCA	Tremors and seizures seen in overdose	Risk of fatal overdose when combined with SSRIs, SNRIs, or clomipramine	Relatively safe in overdose	Relatively safe in overdose	Relatively safe in overdose
Drug Interactions	MAOI, SNRI Some SSRIs (fluoxetine, fluvoxamine, paroxetine) strongly inhibit cytochrome P450 enzymes, therefore will affect levels of drugs metabolized by P450 system	MAOI, SSRI Low inhibition of cytochrome P450 compounds	MAOI, SSRI EtOH	Hypertensive crises with noradrenergic medications (i.e. TCA, decongestants, amphetamines) Serotonin syndrome with serotonergic drugs (i.e. SSRI, SNRI, tryptophan, dextromethorphan)	MAOI Drugs that reduce seizure threshold: antipsychotics, systemic steroids, quinolone antibiotics, antimalarial drugs	MAOI, paroxetine Opioids	MAOI, RIMA	MAOI	MAOI No inhibition of cytochrome P450

Mood Stabilizers

General Prescribing Information

- examples: lithium, divalproex, lamotrigine, carbamazepine
- used mainly for long-term stabilization of bipolar disorder, also used as first-line monotherapy or in conjunction with atypical antipsychotics for acute episodes of bipolar disorder (i.e. depression and mania)
- vary in their ability to "treat" (i.e. reduce symptoms acutely) or "stabilize" (i.e. prevent relapse and recurrence) manic and depressive symptoms; multi-agent therapy can be avoided in many patients but it is common
- before initiating, get baseline: CBC with differential and platelets, ECG (if patient >45 y/o or cardiovascular risk), BUN, creatinine, extended electrolytes, TSH, LFTs for divalproex and carbamazepine
- Also: screen for pregnancy, thyroid disease, neurological, renal, liver, cardiovascular diseases
- full effects may take 2-4 wk, thus may need acute coverage with benzodiazepines or antipsychotics

Specific Prescribing Information

- detailed pharmacological guidelines available online from the Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD)
- for clinical information for treating bipolar disorder (see *Mood Disorders*, PS10)
- be mindful that divalproex and carbamazepine are teratogenic thus if prescribed for women at reproductive age, a reliable contraceptive strategy is required

Table 21. Commonly Used Mood Stabilizers

	Lithium	Lamotrigine (Lamictal®)	Divalproex (Epival®)	Carbamazepine (Tegretol®)
Indications	**1st line** Acute mania (monotherapy or with adjunct SGA) Bipolar I depression (monotherapy or in combination with divalproex, SSRI, or bupropion) Bipolar disorder maintenance (monotherapy or with adjunct SGA) **Other uses** Bipolar II depression Augmentation of antidepressants in MDD and OCD Schizoaffective disorder Chronic aggression, antisocial behaviour Recurrent depression	**1st line** Bipolar I depression (monotherapy) Bipolar disorder maintenance (limited efficacy in preventing mania, more effective when combined with lithium) **Other uses** Bipolar II depression Not recommended for acute mania	**1st line** Acute mania (monotherapy or with adjunct SGA) Bipolar I depression (combination with lithium or SSRI) Bipolar disorder maintenance (monotherapy or with adjunct SGA) **Other uses** Bipolar II depression Rapid cycling bipolar disorder Mixed phase/dysphoric mania	**2nd line** Acute mania (monotherapy) Bipolar disorder maintenance (monotherapy or in combination with lithium) **Other uses** Rapid cycling bipolar disorder
Mode of Action	Unknown Therapeutic response within 7-14 d	May inhibit 5-HT3 receptors May potentiate DA activity	Depresses synaptic transmission Raises seizure threshold	Depresses synaptic transmission Raises seizure threshold
Dosage	Adult: 600-1500 mg/d Geriatric: 150-600 mg/d Usually daily dosing Blood levels monitored and dose adjusted accordingly	Note: very slow titration required due to risk of Stevens-Johnson Syndrome Dose adjusted in patients taking other anticonvulsants such as divalproex Daily dose: 100-200 mg/d	750-2500 mg/d Usually daily dosing with ER preparation	400-1600 mg/d Usually BID or TID dosing
Therapeutic Level	Adult: 0.8-1.0 mmol/L (1.0-1.25 mmol/L for acute mania) Geriatric: 0.6-0.8 mmol/L	Therapeutic plasma level not established Dosing based on therapeutic response	17-50 mmol/L Same therapeutic levels as used for seizure prophylaxis (no data specific for mood stabilizing effect)	350-700 µmol/L Same therapeutic levels as used for seizure prophylaxis (no data specific for mood stabilizing effect)
Monitoring	Monitor serum levels every 5-7 d until therapeutic (always 12 h after dose) Then monitor monthly, then q2-3 mo Monitor thyroid function, creatinine q6 mo	Monitor for skin rash and suicidality when initiating treatment	Monitor serum levels every 5-7 d until therapeutic LFTs weekly x 1 mo, then monthly, then q2-3 mo due to risk of liver dysfunction Watch for signs of liver dysfunction: nausea, edema, malaise Check platelets and monitor levels to adjust dosage and confirm adherence	Monitor serum levels every 5-7 d until therapeutic Weekly blood counts for 1st mo, due to risk of agranulocytosis Watch for signs of blood dyscrasias: fever, rash, sore throat, easy bruising
Side Effects	GI: N/V, diarrhea, stomach pain GU: polyuria, polydipsia, nephrogenic diabetic insipidus, glomerulonephritis, renal failure, decreased glomerular filtration rate CNS: fine tremor, headache, fatigue, lethargy Hematologic: reversible benign leukocytosis Other: teratogenic (Ebstein's anomaly), hypothyroidism, weight gain, edema, worsening of psoriasis, bradycardia, ECG changes	Skin: rash (consider discontinuing due to risk of Steven-Johnson syndrome which is an emergency), slow dose titration to reduce risk Otherwise, usually well tolerated (GI: N/V, diarrhea CNS: ataxia, dizziness, diplopia, headache, somnolence Other: anxiety)	GI: liver dysfunction, N/V, diarrhea CNS: ataxia, drowsiness, tremor, sedation, cognitive blurring Other: hair loss, weight gain, thrombocytopenia, neural tube defects when used in pregnancy, polycystic ovarian syndrome	GI: N/V, diarrhea, hepatic toxicity CNS: ataxia, dizziness, slurred speech, drowsiness, confusion, nystagmus, diplopia Hematologic: transient leukopenia (10%), rare agranulocytosis, aplastic anemia Skin: rash (5% risk; consider discontinuing drug because of risk of Stevens-Johnson syndrome) Other: neural tube defects when used in pregnancy
Interactions	NSAIDs, thiazides, ACEI, and metronidazole decrease clearance, risk for lithium toxicity		OCP	OCP

Lithium Toxicity

- clinical diagnosis as toxicity can occur at therapeutic levels
- common causes: overdose, sodium/fluid loss, concurrent medical illness or initiation of NSAIDs, diuretics, or ACEI
- clinical features
  - GI: severe nausea/vomiting and diarrhea
  - cerebellar: ataxia, slurred speech, lack of coordination
  - cerebral: drowsiness, myoclonus, tremor, upper motor neuron signs, seizures, delirium, coma
- management
  - discontinue lithium for several days and begin again at a lower dose when lithium level has fallen to a non-toxic range
  - monitor serum lithium levels, creatinine, BUN, electrolytes
  - IV saline
  - hemodialysis if lithium >2 mmol/L, coma, shock, severe dehydration, failure to respond to treatment after 24 h, or deterioration

Long-term lithium use can lead to a nephropathy and diabetes insipidus in some patients

Anxiolytics

- anxiolytics mask or alleviate symptoms
- **indications**
  - short-term treatment of anxiety disorders, insomnia, alcohol withdrawal (especially delirium tremens), barbiturate withdrawal, akathisia due to antipsychotics, seizure disorders, musculoskeletal disorders, agitation or aggression associated with acute mania, or psychosis
- **relative contraindications**
  - major depression (except as an adjunct to other treatment), history of drug/alcohol misuse, caution in pregnancy/breastfeeding
  - myasthenia gravis is a relative contraindication for benzodiazepines
- **mechanism of action**
  - benzodiazepines: potentiate binding of GABA to its receptors; results in decreased neuronal activity
  - buspirone: partial agonist of 5-HT1A receptors

Benzodiazepine Antagonist – Flumazenil (Anexate®)
Use for suspected benzodiazepine overdose
Specific antagonist at the benzodiazepine receptor site

Benzodiazepines

- should be used for limited periods (i.e. days-weeks) to avoid tolerance and dependence
- all benzodiazepines are sedating, decrease respiratory drive, and increase risk for falls, confusion, and motor vehicle accidents; be wary with use in the elderly, especially in combination with other psychotropic medications
- have similar efficacy, so choice depends on half-life, metabolites, and route or schedule of administration
- taper slowly over weeks-months because they can cause withdrawal reactions (see below)
- beware of use with alcohol and other CNS depressants because of potentiation of CNS depression; caution with drinking and driving/machinery use
- **side effects**
  - CNS: drowsiness, cognitive impairment, reduced motor coordination (falls), memory impairment
  - dependence, tolerance, withdrawal
- **withdrawal**
  - low dose withdrawal symptoms: tachycardia, HTN, panic, rebound insomnia, anxiety, impaired memory and concentration, perceptual disturbances
  - high dose or rapid withdrawal symptoms: hyperpyrexia, seizures, death
  - onset: 1-2 d (short-acting), 2-4 d (long-acting)
  - duration: days-weeks
  - complication with above 50 mg diazepam/d or abrupt withdrawal: autonomic hyperactivity, seizures, delirium, arrhythmias
  - management: taper slowly, may need to switch to a long-acting benzodiazepine
  - similar to but less severe than alcohol withdrawal; can be fatal
- **overdose**
  - overdose is common but rarely fatal unless combined with other substances
  - more dangerous or potentially fatal when combined with alcohol, other CNS depressants, opioids, or TCAs

Benzodiazepines That are Safe for Patients with Impaired Liver Function

LOT
Lorazepam
Oxazepam
Temazepam

Buspirone (Buspar®)

- primary use: GAD
- may be preferred over benzodiazepines because it is non-sedating, has no interaction with alcohol, does not alter seizure threshold, not prone to abuse
- onset of action: 2 wk
- side effects: dizziness, drowsiness, nausea, headache, nervousness, EPS

Z-drugs for Sleep

- non-benzodiazepine sedatives indicated for short-term management of insomnia
- examples include zopiclone (Imovane®), eszopiclone (Lunesta®), and zolpidem (Sublinox®)
- anecdotally provide a more restful sleep than benzodiazepines
- similar side effect profile and warnings to benzodiazepines
- should not be used long-term due to side effects and likelihood of dependency

Table 22. Dosing and Indications for Common Anxiolytics

Class	Drug	Dose Range (mg/d)	$t_{1/2}$ (h)	tmax (h)	Appropriate Use
Benzodiazepines					
Long-acting	Clonazepam (Rivotril®)	0.25-4	18-50	1-4	Seizure prevention, akathisia, generalized anxiety disorder, panic disorder
	Diazepam (Valium®)	2-40	30-100	1-2	Seizure prevention, muscle relaxant, alcohol withdrawal, generalized anxiety
	Chlordiazepoxide (Librium®)	5-300	30-100	1-4	Alcohol withdrawal
	Flurazepam (Dalmane®)	15-30	50-160	0.5-1	Should be avoided
Short-acting	Alprazolam (Xanax®)	0.25-4.0	6-20	1-2	Should be avoided due to high dependency rate
	Lorazepam (Ativan®)	0.5-6.0	10-20	1-4	Alcohol withdrawal (no first-pass liver metabolism), akathisia, short-term sedation for anxiety during procedures (e.g. CT or MRI), generalized anxiety; sublingual or IM for rapid action
	Oxazepam (Serax®)	10-120	8-12	2-3	Alcohol withdrawal (no first-pass liver metabolism), generalized anxiety disorder
	Temazepam (Restoril®)	7.5-30	8-20	2-5	Should be avoided
	Triazolam (Halcion®)	0.125-0.5	1.5-5	1-2	Shortest $t_{1/2}$, rapid sleep without daytime sedation (e.g. overnight plane travel), but risk of rebound insomnia
Azapirones					
	Buspirone (Buspar®)	15-30	2-3	1-1.5	Generalized anxiety disorder

Somatic Therapies

Electroconvulsive Therapy

- ECT is a safe and controlled way of producing seizures to treat mental illness
- various methodological improvements have been made since the first treatment in 1938 to reduce adverse effects
- modern ECT: induction of a generalized seizure using an electrical pulse through scalp electrodes while the patient is under general anesthesia with a muscle relaxant
- considerations: unilateral vs. bilateral electrode placement, pulse rate, energy, number, and spacing of treatments
- usual course is 6-12 treatments, 2-3 treatments per wk
- indications
  - treatment-resistant depression (unipolar, bipolar I, bipolar II): psychotic features, catatonic features, when medications may be unsafe or rapid response is needed (e.g. cachexia, severe dehydration, frail elderly, high suicide risk, pregnancy)

ECT in Society
Prior to the 1940's, ECT was performed without the use of muscle relaxants, resulting in seizures with full-scale convulsions and rare but serious complications such as vertebral and long-bone fractures. This practice may have led to negative societal perceptions of ECT, further perpetuated by negative depictions in popular culture. Despite ongoing stigmatization, ECT as it is practiced today is an effective and safe option for patients with severe mental illness, including depression

  - catatonia: refractory, severe, or life-threatening
  - schizophrenia: treatment-resistant, acute symptoms, catatonia, history of NMS
  - mania: refractory, severe or life-threatening situation
  - personal or family history of good response to ECT
  - inconclusive evidence for OCD
- adverse effects: risk of anesthesia (equal to risk of ECT), memory loss (may be retrograde and/or anterograde, tends to resolve by 6-9 mo, permanent impairment controversial), transient headaches, transient myalgias
- unilateral ECT causes less memory loss than bilateral but may not be as effective
- contraindications: no absolute contraindications; relative contraindications: increased intracranial pressure, recent (<4 wk) hemorrhagic stroke, recent (<2 wk) MI, requires special monitoring

Electroconvulsive Therapy for Treatment Resistant Schizophrenia
Cochrane DB Syst Rev 2019;CD011847
Purpose: Assess benefits and harms of ECT for people with treatment-resistant schizophrenia.
Outcomes: Moderate-quality evidence indicates that relative to standard care, ECT has a positive effect on medium-term clinical response for people with treatment-resistant schizophrenia. However, there is no clear and convincing advantage or disadvantage for adding ECT to standard care for other outcomes.

Repetitive Transcranial Magnetic Stimulation (rTMS)

- noninvasive production of focal electrical currents in select brain circuits using magnetic induction
- indications: strong evidence for treatment-resistant depression and pain disorders; possibly efficacious for anxiety disorders, PTSD, eating disorders, and substance use disorders
- adverse effects: common – transient local discomfort, hearing issues, or cognitive changes; rare - seizure, syncope, mania induction

Magnetic Seizure Therapy (Experimental)

- magnetic seizure therapy (MST) is generalized seizure induction using strong magnetic current
- early studies demonstrate efficacy for depression as well as anxiety, with reduced memory effects vs. ECT

Neurosurgical Treatments

Ablative/Lesion Procedures

- used for MDD or OCD unresponsive to all other forms of treatment; efficacy ranges from 25-75% depending on procedure
- adverse effects: related to lesion location and size, high-risk of suicide in those who are not helped by surgery
- focused ultrasound therapy (FUS) is an experimental surgical technique under investigation for the treatment of MDD, OCD with the advantage of avoiding an open skull surgery

Deep Brain Stimulation (Experimental)

- placement of small electrode leads in specific brain areas to alter neuronal signaling
- most evidence for treating OCD, some evidence for other disorders such as treatment-resistant MDD
- response rates (>50% symptom reduction) of 40-70%, adverse effects related to surgical risks and poor treatment response

Vagus Nerve Stimulation

- direct, intermittent electrical stimulation of left cervical vagus nerve via implanted pulse generator
- used for chronic, recurrent MDD with poor response to previous therapy and ECT
- slow onset, approximately 30% response rate at 1 yr

Other Therapy Modalities

Phototherapy (Light Box Therapy)

- bright light source exposure (usually 10000 lux) for 30 min daily within the first hour of awakening
- proposed mechanisms: reverses pathological alterations in circadian rhythm through action on suprachiasmatic nucleus
- indications: seasonal affective disorder (SAD), non-seasonal depression (as augmentation), and some sleep disorders
- adverse effects: mania induction, reaction with photosensitizing drug or photosensitive eye or skin conditions

Aerobic Exercise

- moderate-intense aerobic exercise is associated with acute increased release of serotonin, phenethylamine, brain-derived neurotrophic factor, endogenous opioids, and cannabinoids (likely this combination is what contributes to the "runner's high")
- associated with long term increases grey matter in multiple areas, as well as improvements in cognition, memory, and stress tolerance
- indications: monotherapy for mild-moderate MDD; adjunctive therapy for moderate-severe MDD
- may be helpful in PTSD, schizophrenia

Canadian Legal Issues

Common Forms

- the legislation is specific to each province, as are the types and numbers of forms, but the principles are common across Canada

Table 23. Common Forms Under the Mental Health Act (in Ontario)

Form	Who Signs	When	Expiration Date	Right of Patient to Review Board Hearing	Options Before Form Expires
Form 1: Application by physician to bring a patient to hospital (schedule 1 facility) for psychiatric assessment against patient's will (Form 42 given to patient)	Any physician	Within 7 d after having examined the patient	72 h after hospitalization Void if not implemented within 7 d	No	Form 3 and 30 or voluntary admission or send home ± follow-up
Form 2: Order by Justice of the Peace to bring patient to a hospital for an examination against patient's will	Justice of the Peace	No statutory time restriction	7 d from when completed Purpose of form is complete once patient brought to hospital	No	Form 1 and 42 or voluntary admission or send home ± follow-up
Form 3: Certificate of involuntary admission to a schedule 1 facility (Form 30 given to patient, notice to rights advisor)	Any physician other than physician who completed Form 1	Before expiration of Form 1 Any time to change status of a voluntary inpatient	14 d	Yes	Form 4 and 30 or voluntary admission (Form 5)
Form 4: Certificate of renewal of involuntary admission to a schedule 1 facility (Form 30 given to patient, notice to rights advisor)	Any physician, usually the attending physician following patient on Form 3	Prior to expiration of Form 3	First: 1 mo Second: 2 mo Third: 3 mo (max)	Yes	Form 4 and 30 or voluntary admission (Form 5)
Form 4a: Certificate of continuation of involuntary admission to a schedule 1 facility (Form 30 given to patient, notice to rights advisor, Form 17 sent to the Capacity and Consent Board, copies to chart)	Any physician, usually the attending physician following patient on Form 4	Prior to expiration of the third Form 4	3 mo	Mandatory review board hearing	Another Form 4a or voluntary admission
Form 5: Change to informal/voluntary status	Any physician, usually the attending physician following patient on Form 3/4/4a	Whenever deemed appropriate (i.e. the criteria for involuntary admission under the Mental Health Act are no longer fulfilled)	N/A	N/A	N/A
Form 30: Notice to patient that patient is now under involuntary admission on either Form 3, 4, or 4a (original to patient, copy to chart)	Physician issuing the Form 3/4/4a	Whenever Form 3/4/4a filled	N/A	Yes	N/A
Form 33: Notice to patient that patient is incapable of consenting to treatment of a mental disorder, and/or management of property and/or disclosure of health information (original to patient, notice to rights advisor, copy to chart)	Attending physician	Whenever deemed appropriate	N/A	Yes	N/A
Form 42: Notice to the patient that patient is now on a From 1 and the reason for this change (original to patient, copy to chart)	Physician who is signing Form 1	Whenever Form 1 filled	N/A	No	

* Schedule 1 Facilities: Able to provide intensive inpatient and outpatient care

Form 1: Application for Psychiatric Assessment

- Filled out when patients are thought to be in imminent danger to harm themselves (suicide) or others (homicide) or when they are incapable of self-care (e.g. not dressed for freezing weather) and are suffering from an apparent mental disorder
- Based on any combination of the physician's own observations and facts communicated by others
- Box A or Box B completed
- **Box A:** Serious Harm Test
- The Past/Present Test assesses current behaviours/threats/attempts
- The Future Test assesses the likelihood of serious harm occurring as a result of the presenting mental disorder. In this section, one should document evidence of the mental disorder and concerning behaviour/thoughts
- **Box B:** Patients with a known mental disorder, who are incapable of consenting to treatment (substitute decision-maker needed), have previously received treatment and improved, and are currently at risk of serious harm due to the same mental disorder

Consent

- see Ethical, Legal, and Organizational Medicine, ELOM11

CTO Legislature

- Ontario passed CTO legislature on December 1, 2000 (known as "Brian's Law")
- Similar CTOs have been implemented in Saskatchewan (1995), Manitoba (1997), and British Columbia (1999)

Community Treatment Order (CTO)

- purpose: a community treatment order (CTO) orders a person suffering from a serious mental disorder to receive treatment and supervision in the community. Based on a comprehensive plan outlining medications, appointments, and other care believed necessary to allow the person to live in the community (vs. in a psychiatric facility, where conditions are more restrictive)
- intended for those who:
  - due to their serious mental disorder, experience a pattern of admission to a psychiatric facility where condition is usually stabilized
  - after being released, these patients often stop treatment, leading to destabilization
  - due to the destabilization of their condition, these patients usually require readmission to hospital
  - if CTO violated (i.e. treatment not taken), the physician can issue a Form 47 which is an order for examination that allows the police to bring the patient to the hospital for an examination (usually the patient is examined and the treatment will continue as per the CTO)
- criteria for a physician to issue a CTO
  - patient with a prior history of psychiatric hospitalization (cumulative ≥30 d over ≥2 hospitalizations in the past 3 yr), or the person has been subject to a previous CTO in the past 3 yr
  - a community treatment plan for the person has been made
  - examination by a physician within the previous 72 h before entering into the CTO plan
  - ability of the person subject to the CTO to comply with it
  - consultation with a rights advisor and consent of the person or the person's substitute decision maker
- CTOs are valid for 6 mo unless they are renewed or terminated at an earlier date such as
  - when the person or his/her substitute decision-maker withdraws consent to the community treatment plan
- CTO process is consent-based and all statutory protections governing informed consent apply
- the rights of a person subject to a CTO include
  - the right to a review by the Consent and Capacity Board with appeal to the courts each time a CTO is issued or renewed
  - a mandatory review by the Consent and Capacity Board every second time a CTO is renewed
  - the right to request a re-examination by the issuing physician to determine if the CTO is still necessary for the person to live in the community
  - the right to review findings of incapacity to consent to treatment
  - provisions for rights advice

CTO Legislature
- Ontario passed CTO legislature on December 1, 2000 (known as "Brian's Law")
- Similar CTOs have been implemented in Saskatchewan (1995), Manitoba (1997), and British Columbia (1999)

Duty to Inform/Warn

- see Ethical, Legal, and Organizational Medicine, ELOM10

Landmark Psychiatry Clinical Trials

Trial	Reference	Results
Schizophrenia		
CATIE	Psychiatr Serv 2008;59(5):500-506	**Title**: What CATIE Found: Results From the Schizophrenia Trial **Purpose**: Compare the effectiveness of a proxy first-generation antipsychotic (perphenazine) to several second-generation antipsychotics. **Methods**: 1460 patients with chronic schizophrenia were randomly assigned in a double-blind study to receive one of perphenazine, olanzapine, quetiapine, risperidone, or ziprasidone for up to 18 mo. **Results**: Perphenazine did not differ significantly in overall effectiveness or benefits compared to the second-generation antipsychotics. Perphenazine was the most cost-effective drug. Individual clinical circumstances impacted drug effectiveness. Patients who have a poor response to an initial medication may tolerate and see greater effectiveness with a different medication. **Conclusions**: First and second-generation antipsychotics did not differ in overall effectiveness. Patient factors must be considered when prescribing antipsychotic medications.
Major Depressive Disorder		
TRANSFORM-2	Am J Psychiatry 2019,176(6):428-438	**Title**: Efficacy and Safety of Flexibly Dosed Esketamine Nasal Spray Combined With a Newly Initiated Oral Antidepressant in Treatment-Resistant Depression: A Randomized Double-Blind Active-Controlled Study **Purpose**: Evaluate the efficacy and safety of flexibly dosed esketamine nasal spray for patients with treatment-resistant depression. **Methods**: Patients with treatment-resistant depression were randomly assigned treatment of esketamine nasal spray with a newly initiated antidepressant or a placebo nasal spray with a newly initiated antidepressant. **Results**: 197 participants completed the study. Patients receiving the esketamine nasal spray plus antidepressant treatment demonstrated a change in Montgomery-Åsberg Depression Rating Scale score that was significantly greater than placebo nasal spray plus antidepressant at day 28. Clinically meaningful improvements were found in the esketamine group earlier in the study timeline. **Conclusions**: Esketamine nasal spray was a safe, rapid-acting, and efficacious therapy for treatment-resistant depression.

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